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# IRPTC Bulletin

**Journal of the International Register of Potentially Toxic Chemicals**

**devoted to information on hazardous chemicals**

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*Editorial*

### The new Executive Director of UNEP

*In January 1993 Ms. Elizabeth Dowdeswell of Canada arrived in Nairobi, Kenya, and took up her assignment as the new Executive Director of the United Nations Environment Programme (UNEP). On 8 December 1992, the UN General Assembly had elected her for a four-year term, effective 1 January 1993, to head the UN system's environmental conscience – UNEP.*

*Ms Dowdeswell becomes the third Executive Director in UNEP's 20-year history, succeeding Dr. Mostafa K. Tolba, who had retired at the end of last year after serving for 17 years as head of UNEP, beginning in 1976. The first Executive Director was Maurice Strong, most recently the Secretary-General of the UN Conference on Environment and Development (UNCED), who served from 1972 to 1975.*

*Upon her arrival at UNEP's headquarters at Gigiri, Nairobi, where she was greeted by senior members of the organization, she commented that she was 'truly honoured to be joining the ranks of an organization with a role so central to the pursuit of peace as that of the United Nations Environment Programme'.*

*At the time of her election, Ms. Dowdeswell was serving as the Assistant Deputy Minister at Environment Canada and head of the Atmospheric Environment Service – the primary weather and atmospheric agency of the national Government. There she was in charge of a staff of 2,500 and was responsible for transforming that agency by integrating policy development, educational programmes, economic development imperatives and a global vision with its traditional operational public service and scientific research functions.*

*In addition, she has had an extensive experience in the international environment field,*

*particularly as Canada's principal delegate to the Intergovernmental Panel on Climate Change (IPCC) and co-chaired the working group on mechanisms in the negotiations leading to the Framework Convention on Climate Change, which was adopted last June in Rio de Janeiro by UNCED.*

*She has been her country's Permanent Representative to the World Meteorological Organization (WMO), serving twice on its Executive Council. She was also the Canadian Chair of the Great Lakes Water Quality Board for the Canada-United States International Joint Commission.*

*Ms. Dowdeswell, prior to joining the Canadian Environment Ministry, managed a number of public inquiries and Royal Commissions into the country's national unemployment benefits programme, its water policy and the level of weather services.*

*On the provincial level, she achieved the rank of Deputy Minister of Culture and Youth of the Province of Saskatchewan while still in her thirties, a post she held for five years. Her early career also included terms as human rights ombudsman, university lecturer, programme consultant for the provincial department of education and as high school teacher.*

*Ms Dowdeswell's acknowledged commitment to realizing sustainable development has led to invitations to address major gatherings in the developed and developing world. In the past two years, she has addressed meetings of agronomists, engineers, lawyers, educators and scientists in Japan, Italy, the United States, China and Hungary, in addition to her native Canada.*

*Ms Dowdeswell holds a Master of Science degree in behavioural sciences from Utah State University, as well as a Bachelor of Science degree in home economics and a teaching certificate from the University of Saskatchewan, Canada.*

## The Future Course of UNEP

The Executive Director of UNEP, Ms Elizabeth Dowdeswell, contributed the guest editorial to a recent issue of 'The Network' (No. 27, June 1993) in which she expressed the main features and principles of the future course of UNEP, based on statements made during the Seventeenth Session of UNEP's Governing Council. In view of their importance a number of these observations are reproduced below.

UNCED marked a new beginning – for Governments and for UNEP. At Rio, Governments endorsed the concept of sustainable development, making it politically legitimate; committed themselves to a new, frighteningly large Agenda 21; signed Conventions on biodiversity and climate change; called for the creation of a Commission on Sustainable Development; and for UNEP to be strengthened and its role enhanced. UNCED created a new process characterized by inclusiveness, transparency, accountability and consensus-building.

The achievement of sustainable development demands the integration of environment concerns with development. It requires UNEP – which brings environmental expertise to the equation – to establish a relationship with those who bring the knowledge and skills associated with development.

As we define the ecological ground rules for sustainability, we must work on three fronts – science, social consensus and public policy. Our programmes must employ the best science – both natural/physical and social. They must contribute to the behavioural change that brings about social understanding and consensus. They must catalyze effective public policies...

We must also continue to be a focal point for the development and promotion of wise and sustainable management of natural resources. Whether it is the rhino or degraded land, biodiversity or water, UNEP can make the connections that result in solutions...

We are ready and willing to implement our part of Agenda 21. But we must change. In the words of Mahatma Gandhi 'we must be the change we wish to see in the world'. That process of change has begun at UNEP...

Implementing sustainable development demands that we must once and for all work together creatively and constructively in true partnerships at every level. We have hope in what UNEP can contribute to sustainable development. There will be an urgency, a commitment, a new input of energy to the job...

We will justify our existence not by the quantity of resources we throw at a problem but by the calibre of the input we make. We will be an intellectual powerhouse – attracting the 'best and the brightest'. We will be agile, putting our resources where they need to be at the right moment in time, avoiding the build up of a paralyzed bureaucracy. We will display a bias for action, becoming an agent of change – challenging ecologically blind programmes and the veneer of environmental protection. We will deliver tangible improvements in the health of the world's overburdened environments and in the quality of life of all peoples.

I know that I cannot wave a magic wand and instantly transform UNEP but I do want to cause constructive damage to the status quo.

As we move from one world order to another, not yet fully defined, we have heightened expectations and hope.

For peace – a world free of the threat of war. For greater international cooperation. For a better life for every man, woman and child. For a world free from dangers of environmental pollution. For a world that is sustainable...

# I. IRPTC and UNEP activities

## Query-Response Service

IRPTC has operated a Query-Response Service since the receipt of its first request for information in March 1976. Although the service started moderately—at 11 queries a year—it is now answering several queries a day. A personal computer database has made it easier to record and keep track of the queries and permits easy retrievability of information sent previously. During the period covering 1 January to 31 December 1992, 558 queries were received and handled. The growth figures are given in the table below and are depicted in the graphical representation.

*Queries received by IRPTC (1976-1992)*

| Year | Yearly total | Cumulative total |
|---|---|---|
| 1976 | 11 | 11 |
| 1977 | 11 | 22 |
| 1978 | 19 | 41 |
| 1979 | 34 | 75 |
| 1980 | 46 | 121 |
| 1981 | 69 | 190 |
| 1982 | 105 | 295 |
| 1983 | 197 | 492 |
| 1984 | 201 | 693 |
| 1985 | 335 | 1028 |
| 1986 | 292 | 1320 |
| 1987 | 312 | 1632 |
| 1988 | 350 | 1982 |
| 1989 | 450 | 2432 |
| 1990 | 423 | 2855 |
| 1991 | 601 | 3456 |
| 1992 | 558 | 4014 |

The breakdown of the different categories of requests related to source country and subject of query for the period under review is as follows:

developing/industrialized countries: 313/245;
environment/health-related matter: 299/259;
agrochemical/non-agrochemical: 141/417;
specific to legal matters: 155;
specific to waste issues: 61.

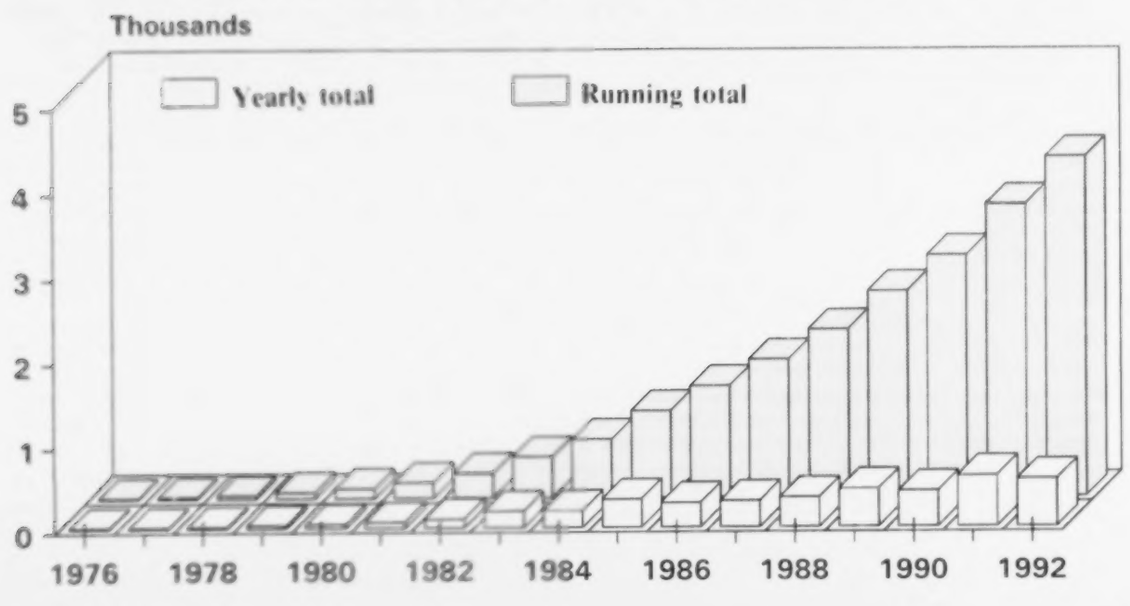
It can be noted that increasing numbers of questions are being received from developing countries – about 56% of the requests. In addition the percentage of questions related to environmental issues is higher than previously.

Queries received still include questions covering several chemicals. There is a general increase in the number of inquiries of a very general nature for which no specific chemical is mentioned. In particular questions of a legislative nature are on the rise. A count of the requests for 1992 shows queries were received from 102 different countries and 16 international organizations.

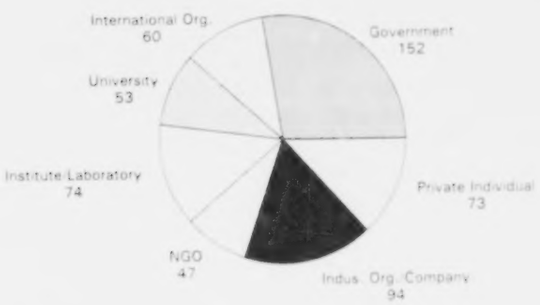
The Query-Response Service records incoming queries by different categories, noting whether it comes from a governmental source, industry, non-governmental organization, academia or a private individual. The pie chart (see next page) provides a breakdown by source for the different categories in 1992.

IRPTC continues to operate its Query-Response Service as one designed primarily to aid national authorities responsible for the protection of human health and the environment, its services being available to everyone at no cost. The Query-Response Service answers to the best of its ability, questions related to aspects of chemicals' identification, use, health and environmental effects, waste disposal and control. Many queries received by IRPTC are complex in nature and difficult to reply to solely using in-

*IRPTC Query-Response Service Trends in queries answered (31 December 1992)*



*REQUEST TYPE*
*(1 January - 31 December 1992)*




formation from its data profiles, although this is one of the prime sources. IRPTC also uses its extensive library, its access to on-line bibliographic information and the IRPTC Bulletin itself. Assistance is also sought from external sources including specialized sectorial sources, international organizations, contributing partners including industry and the IRPTC National Correspondents.

Although IRPTC regularly receives queries related to emergency situations requiring urgent action, it has not been designed to act as a 24-hour emergency response service and it does not have the resources for such an activity. Rather it provides information to those acting on the situation. Recently such situations have been a request from an intergovernmental organization for advice on how to dispose of pesticides spilled due to damage to a storage point during civil strife; a request from the regional office of an intergovernmental organization on the effects of consumption of herbicide contaminated flour; and a governmental request for information on treatment and long-term effects of poisoning due to ingestion of medication contaminated with toxic solvents.

In addition to emergency situations, IRPTC routinely handles requests for basic information on chemicals in its database whether for legislation on a given chemical such as maximum acceptable limits or transport advice or on possible aquatic or terrestrial environmental effect.

The Query-Response Service benefits more than just its users; it is also of value in identifying issues of concern at the global level and in identifying gaps in the information available to IRPTC.

## *Progress in implementation of the FAO/UNEP Joint Programme on Prior Informed Consent (PIC)*

*1. Background*

The Governing Council of UNEP in May 1989 adopted the Prior Informed Consent (PIC) principle and incorporated it into the London Guidelines for the Exchange of Information on Chemicals in International Trade. At about the same time, in November 1989, the 25th Session of the FAO Conference adopted amendments to Articles 2 and 9 of the International Code of Conduct on the Distribution and Use of Pesticides, and introduced the principle of PIC.

Readers will recall that a complete overview of PIC was given in the last issue of the Bulletin (Vol. 11, No. 1&2, 1992, pp. 4-6); the foregoing aims at bringing that information up to date.

*2. Implementation of PIC*

*Appointment of Designated National Authorities (DNAs).* As of January 1993, a total of 156 Designated National Authorities from 116 countries have been registered by the International Register of Potentially Toxic Chemicals (IRPTC) and the Food and Agricultural Organization of the United Nations (FAO). Of the 116 countries participating in the PIC procedure, only a few have limited their participation to that of an exporting country only.

*Issue of 'Guidance for Governments' document on the operation of the PIC procedure.* An operations guide for DNAs entitled 'Guidance for governments on the operation of the PIC procedure' has been prepared by the FAO and UNEP secretariats. This publication is intended to be the main document providing governments with guidance on how the Information Exchange and PIC procedures will operate. It is available in English, French and Spanish. The document has been distributed to all DNAs of participating countries.

*National inventories of control actions to ban or severely restrict chemicals and development of a joint database on banned and severely restricted chemicals.* In order to ensure that the information on control actions in the PIC

## IRPTC National Correspondents

The number of National Correspondents stands at 124 from 116 countries. National Correspondents play an important role in all IRPTC's activities. They possess, and are able to call upon, expertise and experience in the fields of toxicology, public health, occupational health, agriculture, industrial and environmental sciences. As environment is an international disciplinary subject, environmental protection services in most countries are shared among a number of authoritative bodies. Therefore, National Correspondents need to have close links with all these bodies and established direct contact with other institutions and individuals responsible for the control of chemicals in their countries. In addition they assist IRPTC by obtaining information on the following: relevant national legislation and regulations on control of chemical hazards; the existence of national criteria documents, reviews, and reports on chemicals; report on accidents and incidents resulting from loss of chemicals into the environment; and the existence of data banks and other information systems relevant to IRPTC's requirements. They also assist in the operation of the Query-Response Service and are responsible for promoting and distributing of IRPTC publications to interested individuals, institutions, and industries in their respective countries.

In addition, several National Correspondents, have been nominated by their respective governments as Designated National Authorities for the implementation of the amended London Guidelines for the Exchange of Information on Chemicals in International Trade and the Prior Informed Consent procedure.

An updated list of the Register of IRPTC National Correspondents is available from IRPTC.

database is complete and up to date, a letter was sent in September 1991 to all DNAs requesting a national inventory of all control actions to ban or severely restrict chemicals in their country. In addition, a reminder letter was sent in May 1992 to countries which had not yet replied. By 1 October 1992, 41 countries had replied. Some governments have informed that they are not in a position to supply the requested inventory of banned and severely restricted chemicals as they do not at the moment have the necessary legislation to regulate chemicals. Many countries have supplied notifications which are now in the process of being verified for compliance with the definitions and criteria under the procedure. In several cases it will be necessary to contact DNAs again asking for additional information before the data on the control actions can be entered into the PIC database.

In September 1991 the PIC procedure was initiated by distributing the first six DGDs on pesticides (aldrin, DDT, dieldrin, dinoseb and dinoseb salts, fluoracetamide and HCH (mixed isomers)) to all governments. In countries which had appointed more than one DNA, they were advised to coordinate their efforts and provide a joint reply on future import of the chemicals in question. By 1 October 1992 39 countries had responded to the dispatch of the DGDs. Not all countries have however supplied Importing Country Responses for the six pesticides. A reminder letter has also been sent out to governments which have not yet responded.

Another batch of DGDs for six pesticides (chlordane, chlordimeform, cyhexatin, EDB, heptachlor and mercury compounds) was distributed in English on 18 November 1992, and will be distributed in French and Spanish shortly. DGDs for the first five industrial chemicals (polychlorinated biphenyls or PCBs, polychlorinated terphenyls or PCTs, polybrominated biphenyls or PBBs, tris (2,3 dibromopropyl) phosphate and crocidolite) were sent out during February 1993. New chemicals will be identified and corresponding DGDs developed as updated inventories on control actions and new notifications of control actions are received.

As Importing Country Responses are received their replies are entered into the PIC database. The first compilation of Importing Country Responses for the first six pesticides was distributed to DNAs in August 1992. In future they will be distributed on a biannual basis. These listings of import responses should hopefully enable exporting countries to ensure that exports of these chemicals do not take place contrary to the import decisions of the importing country.

### *3. Technical assistance to implement the PIC Procedure, the London Guidelines and the Code of Conduct*

Technical assistance, aimed at all levels, has been extended through TCPs to several countries in Latin America. For the Andean sub-region, a workshop was held with Ecuador as the host country. At Santa Cruz, Bolivia, technical assistance was offered to the faculty and future agronomists at the post-graduate school of the University of Gabriel Rene Moreno. In addition, a workshop on the relevance of the Code of Conduct and the PIC procedure in post-production took place for national personnel of Bolivia. Preparatory technical assistance was given to five countries of the Southern Zone sub-region (Venezuela, Colombia, Bolivia, Peru and Ecuador) on the implementation of the project on harmonization of procedures and regulations for the registration of pesticides in the sub-region.

In response to increasing requests from developing countries for PIC related training and technical assistance activities, UNEP/IRPTC and the United Nations Institute for Training and Research (UNITAR) joined forces in 1991 and established a joint training programme on the implementation of the London Guidelines. The programme has the two main objectives to assist governments in the implementation of the PIC procedure and the establishment of National Registers of Potentially Toxic Chemicals.

Other follow-up activities in the Asian and Pacific Region included a two-week workshop on the establishment of NRPTC's in Thailand, 30 March to 10 April 1992, and the provision of computer equipment to five NRPTCs enabling them to run the PC-version of the IRPTC database. In order to facilitate the cooperation with the industry and trade sector, UNEP and UNITAR organized a regional workshop on the role of industry and trade in implementing PIC, in Cha-am, Thailand, 3 to 5 February 1993.

Plans are now being finalized to extend the UNEP/UNITAR training activities to the Latin American and Caribbean and African regions and it is anticipated that future workshops will increasingly be organized jointly with FAO. The UNEP/UNITAR training programme has received extra budgetary financial support from the Governments of Finland, Netherlands, Switzerland and United States.

### *4. Views of the UNEP Governing Council and FAO Conference*

The UNEP Governing Council at its 16th session in May 1991 requested the Executive Director of UNEP to reconvene the *ad hoc* Working Group on the implementation of the London Guidelines for further urgent action, including work on strengthening the legal basis of the amended London Guidelines, taking into consideration, *inter alia*, experience gained in the implementation of the Guidelines and the PIC procedure. The third session of the *ad hoc* Working Group to review the implementation of the London Guidelines and consider further action took place in Geneva, 25 to 29 January 1993. An informal consultative meeting on modalities to strengthen the legal basis of the amended London Guidelines was held in Geneva from 23 to 25 November 1992.

The 26th Session of the FAO Conference held in November 1991 considered progress achieved in implementation of the Code of Conduct, including the PIC procedure. The general consensus of the conference was that conversion of the Code into a legally binding instrument is premature. The Conference discussed in detail the implementation of the PIC clause under the Code and several members expressed the benefits to be derived from PIC and their satisfaction in the progress made in its implementation. They also commented on the close cooperation and collaborative efforts between FAO and UNEP on PIC.

### *5. Development of model national legislation*

A meeting of legal experts to review draft legislative guidance materials took place in Geneva 28 April to 1 May 1992. Based on the experts' comments and suggestions, two documents (an overview of chemicals management legislation and a supporting module on the implementation of PIC) were further revised. In mid-August both documents were sent to selected reviewers for additional comments.

## *The UNEP List of Selected Environmentally Harmful Chemical Substances, Processes and Phenomena of Global Significance*

The UNEP List of Selected Environmentally Harmful Chemical Substances, Processes and Phenomena of Global Significance was initiated following a decision of the UNEP Governing Council in May 1981 (decision 9/6) to prepare a list of environmentally dangerous chemical substances harmful at the global level, to which special attention should be paid in environmental policies and which would contribute to the formation of public awareness of their possible environmental hazards. Since the original Governing Council decision, the list has been expanded to include harmful processes and phenomena of global significance. The List has been regularly updated, submitted to the Governing Council and circulated to governments, international organizations, industry and non-governmental organizations.

The work of UNEP in general and IRPTC in particular, in close co-operation with other UN and intergovernmental organizations, as well as governments and NGO's, has contributed over the years to encouraging developments leading to improved chemical safety. In the meantime, the concept of the UNEP List has been changing almost imperceptibly. From being originally a 'list' of dangerous chemicals, it moved on to consider the 'processes' involved in the production, use and disposal of chemicals. It moved further, by the very logic of its purpose, to consider the phenomena involved throughout those processes, in recognition of the need for an integrated approach in dealing with impacts and remedies.

The last revision of the UNEP List in Governing Council document UNEP/GC.16/20 contained executive summaries of the chapters on seven major processes and phenomena concerning chemical pollution (pollution due to industrial chemicals, air pollution, acidification, pollution due to agricultural activities, eutrophication, oil pollution and wastes). The results were then combined at the initiative of IRPTC into a monograph *Chemical Pollution: A Global Overview*,[1] giving the scientific background for each issue. This monograph reflects the need for a holistic approach to the problem, rather than the original idea of listing hazardous chemicals and their properties and impacts, and gives a clear assessment of the risks that chemicals present at the global level, as presently understood by the scientific community. UNEP therefore extended its review both to the List as last submitted to the Governing Council and to the more detailed monograph on chemical pollution prepared by IRPTC and GEMS/MARC, UNEP's Global Environment Monitoring System's Monitoring and Assessment Research Centre in the context of the new requirements of UNCED Agenda 21.

By its decision 16/31 of 31 May 1991, the Governing Council requested the Executive Director to again refer the report on the List to governments, relevant international organizations, industry and non-governmental organizations for further study and action as appropriate and to obtain their comments. The decision also requested the Executive Director to review the use made of the List and to submit the results to the Governing Council at its next regular session in 1993. Finally it requested the Executive Director to submit to the Governing Council proposals for a possible update of the List in the light of the outcome of this review.

UNEP sent a questionnaire in February 1992 to governments, international organizations, industry and non-governmental organizations with a view to obtaining their comments on the Executive Summaries of the most recent version of the UNEP List. Replies were received from 25 countries and 16 international organizations. In general it was considered that the List was a useful document and that it was valuable that it continue to be updated.

An expert meeting was convened in January 1993 to prepare proposals for an update. At the same time, analysing the replies received, they noted *inter alia* the following points: that it is necessary to periodically revise the monograph *Chemical Pollution: A Global Overview*; that the revised monograph should clearly include the potential health and environmental consequences of exposure to chemicals; that more quantitative data and an economic cost-benefit evaluation should be included; that the monograph's recommendations should be action oriented; and that the List should be replaced by an assessment of chemical issues critical at the global level.

The follow-up action on these proposals will be reported in a later issue of the *IRPTC Bulletin*.

## *Basel Convention on the Control of Transboundary Movements of Hazardous Wastes*

*First Meeting of the Conference of the Parties*

The First Meeting of the Conference of the Parties to the Basel Convention was held in Piriapolis in December 1992 at the kind invitation of the Government of Uruguay. It was attended by 28 States Parties to the Convention and by the same number of States not Parties, by the European Economic Commission, as well as by observers from 13 international, governmental and non-governmental organizations.

The Conference decided that the second meeting of the Parties shall take place in February/March 1994. The Conference adopted 23 decisions regarding the implementation of the Convention.

The Conference of the Parties requested UNEP to carry out the functions of the permanent Secretariat. Pursuant to this request and effective 1 January 1993, the Executive Director of UNEP has established the Secretariat in accordance with the structure contained in the budget as approved by the Conference for the years 1993 and 1994. The Secretariat is located in Geneva at the invitation of the Swiss Government and as approved by the First Meeting of the Conference of the Parties.

In accordance with Decision 1/7 on Institutional and Financial Arrangements adopted by the Parties, two Trust Funds were established: the Trust Fund for the Basel Convention, with the budget for Implementation of the Convention in 1993 estimated at $1.47 millions, and the Technical Co-operation Trust Fund to Support Developing

[1] Copies of this monograph are obtainable on request from the IRPTC office in Geneva; the Monitoring and Assessment Research Centre, The Old Coach House, Campden Hill, London W8 7 AD, UK; and UNEP Headquarters, P.O. Box 30552, Nairobi, Kenya.

Countries and other countries in need of such assistance to implement the Convention, with the budget of $788,740 for 1993. Parties and non-Parties to the Convention were requested to make their voluntary contributions to both Trust Funds.

The Conference of the Parties has established, by Decision I/2, its Open-Ended *ad hoc* Committee to meet as necessary between the meetings of the Contracting Parties, and also requested the Bureau to work together with the Secretariat between the meetings of the Conference of the Parties.

The main task of the Secretariat, in light of the provisions and principles contained in the Basel Convention, and the Decisions adopted by the First Meeting of the Contracting Parties, is to work towards: reducing transboundary movements of hazardous wastes to a minimum consistent with their environmentally sound management; collecting and disseminating data on the generation of hazardous wastes, their movements and disposal; minimizing the generation of hazardous wastes; ensuring environmentally sound management and disposal of hazardous wastes, aiming at national self-sufficiency in this respect, including preparing technical guidelines for this purpose; providing assistance to Parties, in particular developing countries, in the technical and legal fields covered by the Convention with a view to facilitating the implementation of the Convention; preventing and eliminating illegal traffic in hazardous wastes; preparing a protocol on liability and compensation, including drafting the elements for a compensation fund and emergency funds.

The Conference of the Parties adopted a number of Decisions in particular with regard to the development and adoption of a protocol on liability and compensation, on technical guidelines, on notification and movement documents, on model national legislation, on training activities and establishment of regional centres. The Conference requested industrialized countries to prohibit transboundary movements of hazardous and other wastes for disposal in developing countries and requested developing countries to prohibit the import of hazardous wastes from industrialized countries. Compromise was reached allowing transboundary movements of hazardous waste destined for recovery and recycling provided they are in accordance with the provisions of the Convention. Most of the meeting representatives supported this compromise decision as a first step, although a technical working group is to develop criteria that determine whether such wastes are suitable for recovery operations. The second meeting of the Parties is expected to evaluate the effectiveness of implementation of these decisions in the light of the results of the review of the issue by the Technical Working Group.

A working group was created to further develop a protocol on liability and compensation; the draft presented to the Conference prepared by the Secretariat includes civil liability provisions of unlimited financial liability and, in the case of an illegal shipment, no time limits on liability. The group is also to consider how to establish an international fund to provide for emergency response to accidents involving transport or disposal of hazardous waste. The meeting adopted provisional technical guidelines for the 'environmentally sound management' of solvents, waste oils, polychlorinated biphenyls and domestic waste, as the basis of a formal guideline document. In the context of Agenda 21, a list of priority activities to be carried out was referred to by the Conference focusing particularly on such issues as support to developing countries for strengthening their national capacities in dealing with hazardous wastes including control and prevention of illegal traffic, training and education programmes, monitoring and surveillance systems of transboundary movements, inventories of hazardous waste treatment and disposal sites, health and environmental risks from exposure to hazardous wastes and public information and information dissemination on hazardous waste matters. Several references to the Basel Convention included in Agenda 21, Chapter 20, regarding implementation of the Basel Convention refer also to such issues as protocol on liability and compensation, control procedures, costing and illegal traffic.

The Conference of the Parties requested the Secretariat to further co-operate with the United Nations bodies to achieve the objectives of the Basel Convention, in particular with: (a) the IMO and its Secretariat for the London Convention 1972, as well as with its Maritime Safety Committee and Marine Environment Protection Committee on the development of criteria for the definition of hazardous characteristics; (b) with IAEA in regard to the question of international transboundary movements of radio-active waste and the possibility of developing a legally-binding instrument for the control of these movements; (c) with the Customs Co-operation Council to improve control of hazardous wastes at border points; and (d) with UNIDO, UN Regional Commissions, OECD, EEC, the Commonwealth, and other organizations.

*Work Programme for 1993*

The main activities in 1993 will be to co-operate with and assist Parties in the implementation of the provisions of the Convention and to implement the decisions adopted by the Conference of the Parties at their first meeting. These require the Secretariat to undertake, *inter alia*, the following activities:

—Review of current actions and programmes aiming at identifying, monitoring, preventing, reducing or eliminating illegal traffic in hazardous wastes, with a view to proposing ways and means of enhancing the monitoring and prevention of such traffic; upon assessment of the needs and priorities of a number of Parties for assistance in the identification of illegal traffic, to provide, whenever possible, assistance to them in this field (Decision I/15).

—Finalization of the work on the Protocol on Liability and Compensation including preparation of the elements that would be required for establishing compensation and emergency funds (Decisions I/5 and I/14) and review of existing compensation mechanisms and liability regime work.

—Identification and review of the control procedures applied by States to the transboundary movements of hazardous wastes destined for recovery operations with a view to providing the second meeting of the Conference of the Parties with recommendations on guidelines and procedures with respect to such movements (Decision I/16).

—Review of the provisional technical guidelines already prepared on the environmentally sound management of wastes subject to the Basel Convention and preparation of revised draft technical guidelines (Decision I/19).

—Identification of the needs of Parties in promulgating laws or adapting existing laws or regulations in line with the provisions of the Basel Convention and providing assistance in this regard upon request (Decision I/12).
—Examination of the bilateral, multilateral and regional agreements or arrangements communicated by the Parties to assess their conformity with the provisions of the Convention (Decision I/9).
—Preparation of an analytical summary of the reports submitted by the Parties on the implementation of the Convention (Decision I/11).
—Compilation of information received from developed countries on measures taken to prohibit export of hazardous wastes to developing countries as well as measures taken by the latter to ban import of such wastes (Decision I/22).
—Preliminary assessment of the feasibility of establishing regional centres for training and technology transfer (Decision I/13).
—Preparation of a manual for the implementation of the Convention (Decision I/3).

In addition, the Secretariat shall perform other functions such as mobilizing financial resources to provide, upon request, technical assistance to Parties in need of such assistance in the implementation of the Convention. A technical assistance programme prepared for the Caribbean, for Asia and the Pacific, and West Africa is expected to be funded, in addition to the existing budget, by the Commission of the European Community.

With the Basel Convention, the world community has the opportunity to implement a truly global legal instrument dealing with the control of transboundary movements of hazardous wastes and their disposal.

The Basel Convention could contribute substantially to improving the situation world-wide by reducing transboundary movements and by promoting environmentally sound management of hazardous wastes. The Parties to the Convention should co-operate actively with each other to implement the Convention and, in particular, to assist developing countries in the development of sound management practices and adoption of cleaner production methods. It is therefore of great importance that the provisions of the Basel Convention be implemented as soon as possible, effectively and efficiently, in a spirit of solidarity, to be able to truly contribute to solving hazardous wastes management problems world-wide and to render accessible, practicable and environmentally acceptable options to deal with hazardous wastes.

## *Ad Hoc Working Group of Experts on the Implementation of the Amended London Guidelines*

By decision 15/30 of 25 May 1989, the Governing Council of the United Nations Environment Programme (UNEP) adopted the Amended London Guidelines for the Exchange of Information on Chemicals in International Trade. In accordance with the same decision, the Executive Director convened two sessions of the Ad Hoc Working Group of Experts on the Implementation of the Amended London Guidelines at Nairobi in October 1990 and at Geneva in April 1991 respectively.

As recommended by the Working Group, the Governing Council in its decision 16/35 of 31 May 1991 requested that UNEP undertake further work, including development of model national legislation, consultation with private sector parties in the preparation of a code of ethics on the international trade in chemicals and technical assistance for developing countries to implement the Guidelines.

With a view to implementing the decision, UNEP convened a small meeting of experts on model legislation in Geneva in April 1992 and two consecutive sessions of an informal consultative meeting on a code of ethics on the international trade in chemicals in Geneva and Paris in May and September 1992 respectively.

By the same decision, the Governing Council requested the Executive Director to reconvene the Ad Hoc Working Group for further urgent action, including work on strengthening the legal basis of the Amended London Guidelines, taking into consideration, *inter alia*, experience gained in the implementation of the Guidelines and the prior informed consent (PIC) procedure.

The third session of the Ad Hoc Working Group was held in Geneva from 25-29 January 1993 that was preceded by an informal consultative meeting on modalities to strengthen the legal basis of the Guidelines held in Geneva in November 1992. The meeting was attended by representatives of 49 countries. FAO, UNITAR, the Commission of the European Communities, the Organization for Economic Co-operation and Development, and six non-governmental organizations were represented as observers.

*Recommendations*

Pursuant to the Governing Council decision 16/35 and in recognition of the need to proceed expeditiously in addressing the mandate set forth in Agenda 21, the Ad Hoc Working Group of Experts adopted the following recommendations for transmission to the Executive Director.

1. To finalize and publish legislative guidance documents and ensure their timely and widest possible distribution to assist in the implementation of the Amended London Guidelines.
2. To ensure full utilization of legislative guidance documents by developing countries and countries with economies in transition by providing technical assistance.
3. To develop legislative guidance documents on other aspects of chemicals control.
4. To continue to facilitate the work for preparing a code of ethics on the international trade in chemicals by:
   (i) continuing to provide an international forum for consultation by private sector parties concerned;
   (ii) development of a draft text, based on the work already done.
5. Upon finalization of a code of ethics, to urge governments to enter into commitments with private sector parties to follow the code.
6. To establish a clearing-house mechanism at the international level to match the technical assistance needs of governments with the resources available.
7. To ensure that international organizations, including UNEP and UNITAR, provide training and technical assistance for the implementation of the Amended London Guidelines by addressing the following needs:
   (i) training of government officials to implement the Amended London Guidelines, including

interpretation of the list of PIC chemicals, risk assessment and customs officials;

(ii) assistance for developing chemical legislation, including funding for such purpose;

(iii) appropriate equipment for handling, transporting and storage of pesticides;

(iv) assistance to handle obsolete and out-dated pesticides;

(v) assistance for establishing laboratories and funding for this purpose;

(vi) equipment to implement the PIC procedure such as computers and database;

(vii) assistance in establishing National Registers of toxic chemicals in countries;

(viii) assistance in establishing a technical infrastructure to implement the Guidelines;

(ix) awareness campaigns addressing decision-makers and the public;

(x) training to increase qualification of government officials who handle data and other matters relating to the implementation of the Amended London Guidelines;

(xi) educational programmes to develop human resources to support the infrastructure in the management of chemicals, such as training courses at universities;

(xii) assistance in publishing relevant information and data in local/official language(s) of the respective countries;

(xiii) assistance in disposal of chemical wastes;

(xiv) low-cost technology for safe management of chemicals;

(xv) information on alternatives to banned or severely restricted chemicals and eventual access to such alternatives;

(xvi) research into the environmental effects of use of chemicals in tropical ecosystems.

8. To encourage governments and industry to work together in identifying, evaluating and using safer practical alternatives to hazardous chemicals and widely distribute information on them.

9. To request urgently the Participants Assembly of the Global Environmental Facility to consider modalities for financing technical assistance and training projects needed for the implementation of the PIC procedure.

10. To urge all governments to expeditiously implement the Amended London Guidelines and the PIC procedure.

11. To establish a task force consisting of relevant international organizations, such as UNEP, FAO, WHO, GATT and others in their respective area of competence, and countries, in particular developing countries, to consider modalities for a legally binding instrument for the mandatory application of the PIC procedure.

12. The task force, in its deliberations, shall be guided by the following:

(i) The scope of a legally binding instrument should, for the time being, be limited to the PIC procedure;

(ii) existing instruments in the field of chemicals management, including their implementation, must be taken fully into account.

13. The task force shall:

(i) compile the results of the first year's experience in the full operation of the PIC procedure based on national experiences reported by participating countries;

(ii) evaluate reports provided by governments to determine areas which are successful and unsuccessful under the current implementation of the procedure;

(iii) consider elements necessary for the effective implementation of PIC, including, *inter alia*:

—procedures for the establishment of a designated national authority;

—procedures for export notification;

—procedures for import consent;

—compliance mechanism;

(iv) on the basis of the results of the activities described above, develop legal language designed to achieve the goals of full participation in and implementation of the PIC procedure.

14. To reconvene the Ad Hoc Working Group, within a year, to review the progress in the work of the task force, the provision of technical assistance and training and the implementation of the Amended London Guidelines and the PIC procedure, and report to the Governing Council at its next regular session.

## *Assessing the risk of genetic damage*

Chemicals have contributed significantly to increasing the standard of living of populations around the world. They play a major role in the development of human societies: in agricultural production, in health care, in industry, in transport, in housing and in consumer goods. In recent years, concern has increased over the widespread distribution of chemicals stemming from human activities and their potentially harmful effects on humans and on the ecosystems that sustain us.

Chemicals, as well as ionizing and ultraviolet radiation, can induce permanent genetic alterations in all organisms. These changes, termed mutations, usually have deleterious effects on individuals themselves or on their descendants. The implications of genetic alterations are wide-ranging. In human populations, they may increase the incidences of cancer and genetic diseases. In non-human biota, they may alter the essential balance of an ecosystem or change the virulence of a human pathogen.

Current knowledge about the effects of such agents on human health is limited, and data on their effects on other living organisms are practically non-existent. In order to assess the role of genetic toxicology in determining risks to the genetic integrity of present and future generations of human and non-human biota, the United Nations Environment Programme (UNEP) initiated a joint study 'Assessment of comparative risk associated with exposure of human and non-human biota to genotoxic agents', with the International Commission for Protection against Environmental Mutagens and Carcinogens (ICPEMC).

The major objective of the study was to develop a series of principles and recommendations that may serve as the basis for assessing the genotoxic hazards of environmental agents. It was considered that such principles and recom-

mendations would be useful in setting priorities for the regulation and control of the vast array of chemicals to which humans are exposed in the environment; in formulating guidelines or regulations to mitigate the genetic effects of environmental agents; and in designing appropriate mechanisms to minimize the effects of such agents on both humans and other living organisms.

The management of toxicological risks implies the capacity to control exposure to toxic agents within acceptable safety limits. Effective control depends on prior detection and identification of hazards and the ability to estimate or monitor exposure. Quantitative relationships between low-level exposures to one or several agents and the resulting health effects must also be determined.

Understanding of the underlying mechanisms by which chemical, physical and biological agents produce adverse effects on health and the environment, gained during the last two decades through studies of genetic toxicology, should be involved in the risk assessment process. In addition, efforts should be directed to increasing this understanding and to developing the best methods for applying the knowledge to risk assessment. Such efforts will lead to more realistic determinations of risk, and, if these risks are communicated properly to decision makers and the public, to a more scientific risk management, with the most appropriate results.

A book entitled *Assessing the Risk of Genetic Damage* has been published, based on the working papers that resulted from the study. It is hoped that it will contribute to creating awareness among decision makers and the public of the risks posed by genotoxic agents to human health and that of the environment, so that not only will appropriate preventive measures be taken but also knowledge in this area will continue to improve, with the ultimate aim that the production and use of such agents will be reduced to a minimum.

There are several reasons for attesting to the fact that mutagenic agents are hazardous and that their presence in the environment should be restricted or controlled to the greatest extent feasible.

There is sufficient similarity between the germ-cells of rodents and of humans to assume that human germ-cells can be mutated by chemicals and radiation. In addition, the association between somatic-cell mutagens and germ-cell mutagens in mammals is sufficient to argue that events known to induce damage in genes or chromosomes in human somatic cells may also damage a portion of the germ-cells. Although the quantitative association between mutations in these two cell populations is unknown for most species, this association would be specific for each agent, and it cannot be expressed as a constant.

The relationship between mutations induced in mammalian somatic cells and the development of cancer has been well documented. The induction of mutations at specific sites in some proto-oncogenes and tumour suppressor genes, resulting in transformation of normal cells into tumourous ones, provides a mechanistic basis for this strong association. People with inherited conditions or who have been subjected to environmental exposures that make their DNA unstable, manifested as chromosomal aberrations, also have a high risk for certain cancers.

Identification of an agent as a mutagen in one or more of the currently used tests for genetic toxicity should trigger a series of actions, including: an assessment of the probable exposures of humans and other biota; an assessment of the agent's environmental stability and distribution; and an attempt to determine the potency of the agent to a wide range of organisms. This information can then be used to manage any environmental risk the agent presents. For most mutagens, risk management programmes include: restricting environmental release; taking preventive measures against exposure; and proper labelling. Even with such programmes, organisms with unique hypersensitivity to certain mutagens may still be at risk. The minimal database required for risk management programmes should be identified.

For agents to which there is substantial human exposure but which must be tolerated in the environment, some type of genetic risk assessment is desirable. The methods reviewed in this book are applicable for this purpose. The risk-benefit ratios obtained, including formal risk assessment, are valuable in determining the probable effects of the agent on health and are necessary for proper communication of the risk. However, as the resources required to conduct a genetic risk assessment are considerable, such assessments can be done in only a few circumstances.

One of the few agents that has been studied extensively for genetic risk in both experimental animals and humans is ionizing radiation. Data from those studies are useful for learning how to extrapolate from animal models to the human situation. Results from studies of genetic risk of chemicals cannot, however, be compared directly to results from studies of radiation because of unique factors in the molecular dosimetry of chemicals, i.e., exposure and dose are not related in a constant way, and chemicals undergo metabolism, distribution and excretion. The relationship between the risks due to radiation and those due to chemicals is an area for fruitful future study.

The proper management of genetic risks, associated with exposure to agents that induce mutations in genes or chromosomes should thus be based on what is known about the ability of the agent to reach the DNA of somatic and germ cells and the benefits and associated costs required to control exposure of the target species to the agent.

This publication is available on request from the Environmental Management, UNEP, P.O. Box 30552, Nairobi, Kenya.

*Source: Assessing the risk of genetic damage.* Published by Hodder and Stoughton on behalf of UNEP and ICPEMC (1992).

## *Chemicals Currently being Tested for Toxic Effects*

The International Register of Potentially Toxic Chemicals and the UNEP/ILO/WHO International Programme on Chemical Safety are jointly operating a registry for Chemicals Currently being Tested for Toxic Effects (CCTTE) other than carcinogenicity. This registry contains information on on-going long-term research (Part I). It also contains the registry of critical reviews on chemicals which give information on sources and titles of peer-reviewed documents which are planned, in preparation or have been recently published (Part II).

A chemical review that qualifies for CCTTE is understood to be a document prepared by a group of experts who, after a comprehensive survey of the available literature,

assess the validity of the data contained in it and perform an evaluation of the health and environmental risks posed by the chemical under review. These reviews have been developed by international organizations, national agencies, research institutions, associations of industries or others.

The potential contributors to, and users of, CCTTE are identified as follows:

(i) The relevant agencies of the Member States of UNEP, ILO, WHO and other UN bodies as well as international agencies concerned with chemical safety (e.g. OECD).
(ii) National authorities responsible for toxicological testing and evaluation.
(iii) Industry.
(iv) Scientific institutions and scientists engaged in basic and applied research in toxicology.

The sixth edition of the CCTTE Registry was published January 1993. It contains approximately 480 entries in Part I and 930 in Part II.

**Correspondence**

*Registry of Toxicological Testing*

Please note that the IPCS/IRRU is the centre for the receipt of all data relating to the registry of toxicological testing of chemicals. Inquiries for specific information, and for reporting on new projects or updates of existing studies should be directed to:

IPCS/IRRU
attn: Dr. G. Becking
P.O. Box 12233, MD-A206
Research Triangle Park, NC 27709
USA

Tel: (919) 541-31199
Telex: 802822 WHO RTP

*Registry of Reviews*

Please note that the IRPTC is the centre for the receipt of data related to the 'critical reviews'. Reports of new reviews and copies of completed reviews should be directed to:

The Director
International Register
of Potentially Toxic Chemicals
Case Postale 356
15 Chemin des Anémones
CH-1219 Châtelaine
Geneva
Switzerland

Tel: (022) 979 91 88
Fax: (022) 797 34 60
Telex: 415465 UNE CH

Requests for copies of the 'CCTTE Registry' should also be directed to IRPTC.

## *UNEP/WHO Report on Air Pollution*

Air pollution is posing increasingly serious health problems in some of the world's biggest cities, and is now an almost inescapable part of urban life everywhere, according to a report prepared by the Division of Environmental Health of WHO, the GEMS Monitoring and Assessment Research Centre (London) and the UNEP/GEMS Programme Activity Centre (Nairobi) and published jointly by UNEP and WHO on 1 December 1992.

The report, *Urban Air Pollution in Megacities of the World*, is the result of a scientific study of pollution levels in 20 such cities —those that already have populations of ten million or more, or are expected to reach that total by the year 2000. The United Nations estimates that by then, 47% of the global population will be living in urban areas.

The cities are: Bangkok, Beijing, Bombay, Buenos Aires, Cairo, Calcutta, Delhi, Jakarta, Karachi, London, Los Angeles, Manila, Mexico City, Moscow, New York, Rio de Janeiro, Sao Paulo, Seoul, Shanghai and Tokyo. In some of them, air pollution contributes to premature death and serious disability, the report says, adding that these cities are not necessarily the world's most polluted.

The Director-General of WHO and the Executive Director of UNEP, say in their foreword of the report: 'By studying past and present air pollution problems and air quality management strategies, UNEP and WHO believe that many of the problems currently faced by megacities can be avoided by the megacities of the future'.

The report states that because many of the world's major cities are growing rapidly, with few if any pollution control measures, the hazards will increase and the quality of life for millions of urban residents will continue to fall. To quote: 'It is clear that air pollution in many of the world's megacities, as well as in other cities, is a major health and environmental concern. This concern is increasing and should command high priority for action.'

The study investigated levels of six major pollutants in 20 megacities. The pollutants are: sulphur dioxide ($SO_2$), mainly from power generation and industrial emissions; suspended particulate matter (SPM), largely from domestic fires, power generation and industries; lead (Pb), chiefly from petrol engine exhaust; carbon monoxide (CO), also from motor vehicles; and nitrogen dioxide ($NO_2$) and ozone ($O_3$), due to the combination of heavy traffic and high levels of sunshine.

The basis of pollution control strategies relies on local, national and regional authorities setting air quality and emission standards. By requiring adherence to such standards, governments can better encourage industry to develop new and better technologies to reduce industrial emissions. But the cost of such technologies is beyond the scope of many developing countries, the report states.

The report's recommendations include the urgent implementation, where necessary, of measures such as:

—air quality management programmes;
—energy conservation;
—motor vehicle examination and maintenance programmes;
—phasing out lead in petrol;
—promotion of mass transit systems;
—alternatives to open burning of refuse;
—the introduction of 'clean' technologies.

*Source:* 'Air pollution a serious health risk in some of the world's biggest cities.' Press release issued by WHO/UNEP. 1 December 1992.

# II. International and National activities

## International Agency for Research on Cancer

### I. Chromium, nickel and welding

The forty-ninth volume of *IARC Monographs* covers chromium and its compounds, nickel and its compounds and occupational exposures in welding. Chromium and nickel are widely used as components of stainless steel and other high alloy steels. Even though mild steel is the most common material welded, a considerable proportion of welders are regularly or occasionally exposed to fumes from stainless steel containing chromium and nickel compounds.

Chromium and its compounds have been evaluated previously in the *Monographs* (IARC, 1973, 1979, 1980, 1982, 1987). The monograph on chromium and chromium compounds is, for practical purposes, divided into subsections, on the basis of the oxidation state and solubility of the compounds. The principal oxidation states of chromium are 0, III and VI; in addition, oxidation states II, IV and V occur, and sometimes the agents tested were of mixed or unknown oxidation states. The latter are described under the title 'other chromium compounds'. The compounds tested for carcinogenicity are described in more detail than other compounds of the group in sections on chemical and physical properties, production, use and occurrence. Welding of stainless steel with exposure to chromium is described in detail in the monograph on welding and is cross-referenced in the monograph on chromium and chromium compounds.

In general, stainless-steel welders (mostly fabricators) are exposed primarily to fumes that differ from those in mild-steel welding mainly in their comparatively high content of chromium and nickel. Mild-steel welders work on a variety of materials in a range of situations (e.g., shipyards, construction work), which lead to exposure to a range of particulates such as fume, grinding dust and asbestos and to gaseous substances (e.g., from pyrolytic decomposition of antirust paint on construction plates and the oxides of nitrogen).

Nickel and its compounds have also been evaluated previously (IARC, 1973, 1976, 1979, 1982, 1987). As for chromium, the present monograph on nickel and nickel compounds has been divided into subsections. The purpose of this subdivision was prompted by the fact that since a wide variety of nickel compounds have been tested for carcinogenicity, a grouping of data on individual nickel compounds would be useful. The studies on stainless-steel welding and on welders exposed to nickel are described in the monograph on welding. These studies are, however, cross-referenced in the monograph on nickel and nickel compounds when they are considered to contribute to the evaluation of nickel and its compounds.

Welding and welding fumes have not been evaluated previously, although some of the studies on welders are reviewed in the monographs on chromium and nickel. The chemical composition of welding fumes and gases is determined by the material being welded (e.g., mild steel, stainless steel, aluminium) and the welding technique used (manual metal arc, metal inert gas, tungsten inert gas). When painted steel is welded, the basic components of welding fumes —the metals, metal oxides and metal salts— may be accompanied by a complex mixture of other compounds. In addition to welding fumes and gases, welders are also often exposed to ultraviolet light (IARC, 1986), to electromagnetic fields and, in some cases, to other agents originating from their work (e.g., grinding dust) or from other work carried out at the same place (e.g., asbestos in shipyards).

The epidemiological studies summarized in the monograph on welding were selected on the basis that the majority of the population under study probably consisted of welders. For example, if the occupational group studied was specified as 'welders and solderers', the study was included because the number of solderers is usually much lower than that of welders. On the other hand, studies on 'metal workers' and 'sheet metal workers' were excluded, although in these wide occupational categories there is a minority of persons who are involved in welding operations. Similarly, it is probable that the studies on 'welders' as an unspecified occupation may have included a fair number of stainless-steel welders. It should be noted that laboratory experiments with samples of welding fume may not reflect, in terms of chemical composition, human exposures during the welding process.

*Solubility.* Chromium and nickel compounds are often classified as 'soluble' or 'insoluble'. Such a classification can be useful for describing the physical properties and industrial applications of the various compounds, but has sometimes also been used as a crude index of bioavailability in toxicological investigations. Some confusion has arisen because the terms 'soluble' and 'insoluble' have not always been defined adequately and because a variety of test methods have been used. In the preparation of the monographs in this volume, use was made of the accepted physical definition of 'solubility' in terms of the equilibrium concentration of a single chemical substance in saturated solution in a specified solvent at a given temperature. The 'soluble fraction' of a substance or mixture is usually measured by leaching the substance for a specified time under defined test conditions, and the results obtained are highly dependent upon the precise method used. It should be noted that different forms of nominally the same compound can have very different solubilities and rates of dissolution, and the dissolution rate is affected by particle size, purity and crystallinity.

The dissolution process can involve physical and chemical mechanisms, and the resulting compounds in solution might be chemically different from the source compound in the test material. For example, nickel subsulphide ($Ni_3S_2$) can be oxidized by dissolved oxygen, entering solution as nickel sulphate. Interpretation of the results of leaching measurements can be difficult: a low result, for example might imply either a mixture with a small soluble fraction or a pure soluble material which dissolves relatively

slowly. In few cases can the results of such tests, or data on solubility, for a substance in one solvent system be extrapolated reliably to other solvent systems.

*Bioavailability.* 'Bioavailability' is a term used to denote the fraction of a substance that is absorbed, delivered to a target site and/or is responsible for a specific toxic or carcinogenic effect. Clearly, water solubility of an agent will often be an important factor in its availability within the body. It is, however, not the only relevant determinant of bioavailability. All dissolved chromium species, for example, may not pass equally through cell membranes: chromates in solution readily cross cell membranes, while Cr[III] does not. Chromates, moreover, have a range of solubilities in water and in body fluids, and agents such as lead chromate may release very few chromate ions for passage through cell membranes. Passage through cell membranes is only one route by which an agent may reach a target within a cell: particulate compounds of chromium and nickel may be phagocytized and thus become bioavailable.

The bioavailability of a potentially carcinogenic entity that is common to other members of its class of closely related compounds is an important factor in its carcinogenic potency, as demonstrated by differences in the levels of carcinogenic response observed in experimental and epidemiological studies. Not only is sufficient delivery of metal ion important, but in excess it can produce toxic effects (e.g., inhibitory phagocytosis), limiting uptake or survival of preneoplastic cells.

The classification scheme used in the *IARC Monographs* is qualitative and is based solely on the strength of evidence from the studies considered. Because of differences in observed levels of carcinogenic response, potency, and therefore dissolution and bioavailability as well, play a role in this qualitative evaluation. Alternatively, differences in the degree of evidence may merely reflect the fact that the entity has not been adequately tested over the range of compounds in which it occurs.

*Biological monitoring.* Biological monitoring of chromium, nickel and welding exposures shows that absorption into the human body has taken place. Such studies were considered, but several factors, such as sampling time, toxicokinetic factors and analytical validity, were taken into account, and the Working Group did not attempt to use such data to compare absorbed doses in different exposure situations.

*Availability and reporting of data.* There is a paucity of evidence for and against the possible carcinogenic hazards of oral exposures to chromium or nickel compounds in foods or potable water. There is also a lack of precision in characterizing the chemical species and physical properties of the tested compounds and welding processes described in these monographs, which hinders interpretation of the data.

*Adequacy of animal experiments.* Chromium and nickel are major world commodities, and these metals and their compounds constitute occupational exposures, principally by inhalation, for many millions of workers. Many long-term tests for carcinogenesis have been carried out by application to internal tissues (by injection or implantation); however, few bioassays of exposure by inhalation were available for evaluation. The paucity of data on the effects of inhalation of these compounds is partially offset by evidence from studies by intratracheal and intrabronchial exposure.

Carcinogenic effect is often strongly related to duration of exposure, in both humans and animals; thus, negative results for a single application of a soluble compound in an animal experiment cannot provide reasonable evidence that an agent will not be carcinogenic under conditions of prolonged or repeated application. This fact may provide a possible explanation for some of the negative results observed. In the absence of data from studies of soluble, acutely toxic substances by prolonged inhalation, some evidence may be obtained from repeated exposure of the same target cell population, as by repeated multiple injections of a toxic nickel-containing compound into the peritoneal cavity. The requirements for the carcinogenicity testing of metals need further elaboration.

*Genetic and related effects.* Most of the available short-term test results have been incorporated in the text. These include the results of anchorage-independent growth assays using Syrian hamster BHK21 fibroblasts. This assay in particular demonstrated that many metal compounds can induce changes in the normal growth pattern of the cells; however, neither this assay nor that for foetal mouse cell transformation was evaluated for the final summary, because technical and interpretative difficulties are associated with both of them.

*Interpretation of moderately elevated lung cancer rates.* Apparently moderate elevations in lung cancer rates among occupationally exposed groups may occur as a result of confounding exposures to cigarette smoke and other carcinogens. Accurate smoking histories are rarely available in epidemiological studies of industrial workers, and due to the differences in smoking prevalences, national or even regional lung cancer rates may not provide an appropriate basis for calculating expected numbers in industrial cohort studies. Furthermore, workers in a particular industry may also be exposed to carcinogens in other occupations during their working lives. For example, in several recent industrial studies, high lung cancer rates have been reported among short-term workers, which seem unlikely to be due to the specific period of employment. In the absence of an increasing trend with duration of exposure, a relative risk for lung cancer lower than about 1.5 should be interpreted with caution, although larger excesses are unlikely to be due entirely to smoking or to other exposures.

*Evaluation of the carcinogenicity risk*

*Chromium and its compounds.* There is *sufficient evidence* in humans for the carcinogenicity of chromium[VI] compounds as encountered in the chromate production, chromate pigment production and chromium plating industries.

There is *inadequate evidence* in humans for the carcinogenicity of metallic chromium and of chromium[III] compounds.

There is *sufficient evidence* in experimental animals for the carcinogenicity of calcium chromate, zinc chromates, strontium chromate and lead chromates.

There is *limited evidence* in experimental animals for the carcinogenicity of chromium trioxide (chromic acid) and sodium dichromate.

There is *inadequate evidence* in experimental animals for the carcinogenicity of metallic chromium, barium chromate and chromium[III] compounds.

The Working Group made the overall evaluation on chromium[VI] compounds on the basis of the combined results of epidemiological studies, carcinogenicity studies

in experimental animals, and several types of other relevant data which support the underlying concept that chromium[VI] ions generated at critical sites in the target cells are responsible for the carcinogenic action observed.

The overall evaluation[1] is that chromium[VI] *is carcinogenic to humans* (Group 1) and metallic chromium and chromium[III] compounds *are not classifiable as to their carcinogenicity to humans* (Group 3).

*Nickel and its compounds.* There is *sufficient evidence* in humans for the carcinogenicity of nickel sulphate, and of the combinations of nickel sulphides and oxides encountered in the nickel refining industry.

There is *inadequate evidence* in humans for the carcinogenicity of metallic nickel and nickel alloys.

There is *sufficient evidence* in experimental animals for the carcinogenicity of metallic nickel, nickel monoxides, nickel hydroxides and crystalline nickel sulphides.

There is *limited evidence* in experimental animals for the carcinogenicity of nickel alloys, nickelocene, nickel carbonyl, nickel salts, nickel arsenides, nickel antimonide, nickel selenides and nickel telluride.

There is *inadequate evidence* in experimental animals for the carcinogenicity of nickel trioxide, amorphous nickel sulphide and nickel titanate.

The Working Group made the overall evaluation on nickel compounds as a group on the basis of the combined results of epidemiological studies, carcinogenicity studies in experimental animals, and several types of other relevant data, supported by the underlying concept that nickel compounds can generate nickel ions at critical sites in their target cells.

The overall evaluation is that nickel compounds *are carcinogenic to humans* (Group 1), and, metallic nickel *is possibly carcinogenic to humans* (Group 2B).

*Welding fumes and gases.* There is *limited evidence* in humans for the carcinogenicity of welding fumes and gases.

There is *inadequate evidence* in experimental animals for the carcinogenicity of welding fumes.

The overall evaluation is that welding fumes *are possibly* carcinogenic to humans (Group 2B).

[1] *Group 1: The agent (mixture) is carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans.* This category is used only when there is *sufficient evidence* of carcinogenicity in humans.

*Group 2B: The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans.* This category is generally used for agents, mixtures and exposure circumstances for which there is *limited evidence* of carcinogenicity in humans in the absence of *sufficient evidence* of carcinogenicity in experimental animals. It may also be used when there is *inadequate evidence* of carcinogenicity in humans or when human data are nonexistent but there is *sufficient evidence* of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is *inadequate evidence* of or no data on carcinogenicity in humans but *limited evidence* of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

*Group 3: The agent (mixture, exposure circumstance) is not classifiable as to its carcinogenicity to humans.* Agents, mixtures and exposure circumstances are placed in this category when they do not fall into any other group.

*Source: IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans: Chromium, Nickel and Welding.* Vol. 49, IARC, Lyon, France (1990).

## *II. Chlorinated drinking-water; chlorination by-products; halogenated compounds; cobalt and cobalt compounds*

In this fifty-second volume of *IARC Monographs* evaluations are made of the evidence in relation to the carcinogenicity of chlorinated water supplies, of chemical by-products of the chlorination of drinking-water, of some other chemicals found in drinking-water and of cobalt and cobalt compounds. By-products of the chlorination process found in chlorinated drinking-water that have been evaluated previously in the *IARC monographs* are listed below.

| Compound | Year | Degree of evidence for carcinogenicity | | Overall evaluation of carcinogenicity to humans |
|---|---|---|---|---|
| | | Human | Animal | Group[1] |
| Acetaldehyde | 1987 | I | S | 2B |
| Chloroform | 1987 | I | S | 2B |
| 2,4-Dichlorophenol (see Chlorophenols) | 1986 | L | — | 2B |
| Formaldehyde | 1987 | L | S | 2A |
| 2,4,6-Trichlorophenol | 1987 | L | S | 2B |
| Pentachlorphenol | 1990 | I | S | 2B |

I, inadequate evidence; S, sufficient evidence; L, limited evidence.

### *Chlorinated drinking-water*

The maintenance of an adequate supply of unpolluted water is a requirement for both human health and good environmental quality. Our demands upon the planet's water are great, and in some regions dangerously so. Water

[1] *Group 2:* This category includes agents, mixtures and exposure circumstances for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is experimental evidence of carcinogenicity. Agents, mixtures and exposure circumstances are assigned to either 2A (probably carcinogenic) or 2B (possibly carcinogenic) on the basis of epidemiological, experimental and other relevant data.

*Group 2A: The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans.* This category is used when there is *limited evidence* of carcinogenicity in humans and *sufficient evidence* of carcinogenicity in experimental animals. Exceptionally, an agent, mixture or exposure circumstance may be classified into this category solely on the basis of *limited evidence* of carcinogenicity in humans or of *sufficient evidence* of carcinogenicity in experimental animals strengthened by supporting evidence from other relevant data.

*Group 2B. The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans.* This category is generally used for agents, mixtures and exposure circumstances for which there is *limited evidence* of carcinogenicity in humans in the absence of *sufficient evidence* of carcinogenicity in experimental animals. It may also be used when there is *inadequate evidence* of carcinogenicity in humans or when human data are nonexistent but there is *sufficient evidence* of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is *inadequate evidence* of or no data on carcinogenicity in humans but *limited evidence* of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be place in this group.

*Group 3: The agent (mixture, exposure circumstance) is not classifiable as to its carcinogenicity to humans.* Agents, mixtures and exposure circumstances are placed in this category when they do not fall into any other group.

is taken for drinking, irrigation and industry and is returned as industrial discharge , agricultural run-off and microbiologically contaminated, treated or untreated sewage. Water quality varies according to these discharges, the seasons and the geology of an area. The most critical characteristic of water for human health is its microbiology.

The microbiological quality of water can be controlled effectively by disinfection methods, which normally involve the introduction of chemical oxidants to the water supply. Chemicals used on a substantial scale as disinfectants are chlorine, hypochlorite, chloramine, chlorine dioxide and ozone. Chlorination is almost universally accepted as the method of choice for purifying water supplies. It was first used on a continuous basis for this purpose at the beginning of the twentieth century. It is also used for sewage treatment in a few countries. Since some water suppliers have difficulty in maintaining acceptable water quality, particularly with regard to taste and odour, chlorine may be used in combination with ozone, chlorine dioxide, ammonia and activated charcoal. These treatments are sometimes followed by dechlorination, for example with sulphur dioxide.

There are substantial and irrefutable benefits of disinfection of water supplies by chlorination. Any major change to these programmes would need to be evaluated fully as to its costs and benefits with regard not only to the need to maintain microbiological safety but also to the possible long-term adverse effects of alternatives to chlorination. Nonetheless, it is now known that the interaction of chlorine with naturally occurring humic and fulvic acids in water supplies results in the formation of by-products such as trihalomethanes, halogenated acids and aldehydes, some of which are either known or suspected carcinogens. Other compounds that occur at much lower concentrations include substances that are mutagenic primarily in bacterial and *in vitro* systems but have not been demonstrated to produce cancer in man or experimental animals.

The investigation of possible risks of cancer from consuming chlorinated drinking-water in human populations is difficult. There are a number of methodological obstacles. Chlorination may produce quite different profiles of chemical by-products in different areas. Characterization of a person's water consumption is complicated by the fact that in some parts of the world people change residence during life, and the nature of their domestic water source changes in consequence. Furthermore, people may consume water not only at home but also at work and in other places, and may drink unchlorinated water, bottled water, boiled water and other liquids, which will greatly influence their exposure to chlorination by-products. Exposure to constituents of water other than by ingestion—by inhalation or skin absorption—may also occur. Even if associations can be demonstrated between human cancer risk and exposure to residential chlorinated water supplies, they may be due to other constituents of the water that is chlorinated or to particular characteristics of the populations who live in areas served by chlorinated water supplies.

Evaluation of chlorinated water for carcinogenicity in experimental animals is similarly challenging. Indeed, few studies have yet been conducted in which the effects, if any, of constituents of chlorinated water have been compared with those of constituents of water from the same supply collected before chlorination.

*Evaluation of the carcinogenicity risk given in these monographs*

| Agent | Degree of evidence of carcinogenicity | | Overall evaluation of carcinogenicity to humans |
|---|---|---|---|
| | Human | Animal | Group[1] |
| Bromodichloromethane | I | S | 2B |
| Bromoethane | ND | L | 3 |
| Bromoform | I | L | 3 |
| Chlorinated drinking-water | I | I | 3 |
| Chlorodibromomethane | I | L | 3 |
| Chloroethane | ND | L | 3 |
| Cobalt and cobalt compounds | I | | 2B |
| Cobalt metal powder | | S | |
| Cobalt-aluminium-chromium spinel | | I | |
| Cobalt-chromium-molybdenum alloys | | L | |
| Cobalt[II] oxide | | S | |
| Cobalt[II] sulphide | | L | |
| Cobalt[II] chloride | | L | |
| Cobalt[II,III] oxide | | I | |
| Cobalt naphthenate | | I | |
| Cobalt[III] acetate | | I | |
| Halogenated acetonitriles | | | |
| Bromochloroacetonitrile | ND | I | 3 |
| Chloroacetonitrile | ND | I | 3 |
| Dibromoacetonitrile | ND | I | 3 |
| Dichloroacetonitrile | ND | I | 3 |
| Trichloroacetonitrile | ND | I | 3 |
| Hypochlorite salts | ND | I | 3 |
| Sodium chlorite | ND | I | 3 |
| 1,1,2-Trichloroethane | ND | L | 3 |

I, inadequate evidence; S, sufficient evidence; L, limited evidence, ND, no data.

This volume includes monographs related to the chlorination rather than other methods of disinfection of water, because, firstly, chlorination is the most commonly used disinfection process, and, secondly, potentially carcinogenic by-products have been measured in chlorinated water (although not uniquely so, as they have also been identified in water disinfected by other methods).

*Cobalt and cobalt compounds*

Some explanation is necessary with regard to the inclusion of a monograph on cobalt and cobalt compounds in this volume. It was originally prepared for inclusion in Volume 49 of the *Monographs (Chromium, Nickel and Welding)*; however, during the preparation of that meeting, it became clear that there would be insufficient time to consider this topic adequately. Consequently, it was decided to postpone the evaluation of cobalt and cobalt compounds until the earliest convenient *Monographs* meeting, which was the present one.

Cobalt has widespread and important uses, particularly in alloys with chromium, nickel and several other metals, and it is therefore a component of some industrial environments. Alloys that contain cobalt in combination with chromium, molybdenum, nickel, tungsten and other metals are commonly used in orthopaedic prostheses and in other implanted medical or dental devices. Since, on a worldwide basis, hundreds of thousands of patients receive such implants each year, concern has arisen about the potential carcinogenic hazards of wear particles and of cobalt and other metals that are gradually solubilized from the surface of implants.

Cobalt is a component of an essential micronutrient, vitamin $B_{12}$ (cyanocobalamin), which is synthesized by certain microorganisms and ingested in the diet of humans and animals. However, since the kinetics and metabolism of vitamin $B_{12}$ are distinct from those of other cobalt compounds, it was decided not to consider vitamin $B_{12}$ itself. Similarly, except for cobalt naphthenate, which is widely used industrially, other organic cobalt compounds have not been considered.

*Source: IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans, Chlorinated Drinking Water, Chlorination By-Products, Some other Halogenated Compounds, Cobalt and Cobalt Compounds.* Vol. 52, IARC, Lyon, France (1991).

## *International Programme on Chemical Safety*

### *I. 'Environmental Health Criteria' documents*

The International Programme on Chemical Safety under the joint sponsorship of UNEP, ILO and WHO has published 'Environmental Health Criteria' documents on diethylhexyl phthalate, isobenzan and trichlorfon.

These documents are based on a comprehensive search of available original publications, scientific literature and reviews, and examine the physical and chemical properties and analytical methods, sources of environmental and industrial exposure and environmental transport; chemico-biokinetics and metabolism including absorption, distribution, transformation and elimination; short- and long-term effects on animals (carcinogenicity, mutagenicity and teratogenicity), and finally an evaluation of risks for human health and the effects on the environment.

Summaries of the documents are published in this issue of the Bulletin in the section 'News about Chemicals'.

### *II. 'Health and Safety Guides'*

The 'Environmental Health Criteria' documents (see above) provide guidance for setting exposure limits consistent with the protection of human health and the environment. In order to facilitate the application of these guidelines in national chemical safety programmes, IPCS decided to publish summaries of the criteria documents in the form of 'Health and Safety Guides'. Those published since the last issue of the Bulletin (Vol. 11, No. 1 & 2) are:

74. Parathion
75. Methyl parathion
76. 1,3-Dichloropropene, 1,2-dichloropropane and mixtures
77. Propachlor

Copies of the 'Health and Safety Guides' are available on request from: Sales and Distribution Division, World Health Organization, CH-1211 Geneva 27, Switzerland.

## *United Nations*

### *Convention on Chemical Weapons*

In a major step towards achieving a global ban on chemical weapons, the Conference on Disarmament adopted and transmitted to the 47th UN General Assembly the text of a 24-article Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction, with its annexes (on chemicals, verification and confidentiality) and a text on the preparatory commission for an organization for the Prohibition of Chemical Weapons. Approval of the final draft of the Convention by the Disarmament Conference signified the conclusion of more than ten years of negotiations among delegates of the UN Member States.

The Convention totally prohibits chemical weapons and any activities aimed at or contributing to their use. The ban extends not only to chemical warfare agents as such, but also to the means of delivery. By the Convention, States parties are obliged to destroy all chemical weapons, including those abandoned, and chemical weapons production facilities. Routine as well as short notice 'challenge' inspections of government and industrial facilities are to be conducted to verify compliance. Built-in safeguards, including sanctions, deal with situations where basic obligations are not respected.

To implement the Convention, an organization for the prohibition of chemical weapons is to be established at The Hague, Netherlands. The following is an overview of some important provisions of the Convention.

Under *Article I*, each State party undertakes: never under any circumstances to develop, produce, otherwise acquire, stockpile or retain chemical weapons, or transfer them, directly or indirectly, to anyone; to use or engage in any military preparations to use chemical weapons; and to assist, encourage or induce, in any way, anyone to engage in any activity prohibited under the Convention.

Each State party is obliged to destroy chemical weapons and such production facilities it owns or possesses or that are located in any place under its jurisdiction or control, as well as all chemical weapons it may have abandoned on

the territory of another State party. Each State party will use riot control agents as a method of warfare.

*Article II* defines "chemical weapons", "toxic chemicals", "precursor", "old" and "abandoned" chemical weapons, "riot control agents", "chemical weapons production facility" and "production capacity".

Under *Article III*, each State party will submit to the Organization, not later than 30 days after the Convention enters into force, declarations with respect to chemical weapons and their facilities, specifying their precise location and quantity and providing a general plan for their destruction.

*Articles IV* and *V* contain detailed and rigorous provisions governing the destruction of chemical weapons and their production facilities, including verification. Complete destruction would be required within ten years. Should a State party, in exceptional cases, for technological, financial, ecological or other reasons not be in a position to do so, the Convention would allow for the possibility of extending that time frame by up to five more years. Furthermore, in exceptional cases of "compelling need", Article V permits States parties to convert, rather than destroy chemical weapons production facilities, but only under strict conditions preventing possible reconversion and rigorous additional verification measures.

*Article VI*, in conjunction with the Verification Annex, sets forth a comprehensive and graduated regime for international monitoring, through declarations and on-site inspections, of "activities not prohibited under the Convention", in particular in the chemical industry.

*Article VII*, on national implementation measures, outlines general undertakings and relations between the State party and the organization to be set up under the Convention. *Article VIII* establishes the Organization for the Prohibition of Chemical Weapons at The Hague, to ensure the implementation of the Convention. The Organization will comprise a Conference of the States parties composed of all Member States, which will be the principal organ; the Executive Council with a membership of 41 States parties; and a Technical Secretariat headed by the Secretary-General.

Procedures for consultative clarification and short-notice "challenge inspections" are set forth, in conjunction with the Verification Annex, in *Article IX*.

*Article X*, on assistance and protection against chemical weapons, provides built-in safeguards of the Convention to protect States parties against the hypothetically continuing risk of being threatened or attacked by chemical weapons. It provides for the establishment of a voluntary fund for assistance by the Conference of States parties, for assistance through the Organization in case of the use or threat of use of chemical weapons against a State party, and for immediate emergency assistance directly from other States parties.

*Article XI* aims at promoting expanded international trade, technological development and economic cooperation in the chemical sector for purposes not prohibited under the Convention.

*Article XII* is considered the principal safeguard of the Convention to protect States parties against violations of the basic obligations by other States parties. It provides the means to remedy any situation which contravenes the provisions of the Convention. For example, the Organization may require a State party deemed not to be in full compliance with the Convention to take remedial action and, in the event it fails to do so, apply a number of penalties, including sanctions. In cases of particular gravity, the Conference of States parties would bring the issue to the attention of the General Assembly and the Security Council.

The remaining 12 articles of the Convention deal with its relation to other international agreements, settlement of disputes, amendments, duration of the Convention and withdrawal of a State party, status of the annexes, signature, ratification, accession, entry into force, reservations, depositary and authentic texts.

The Convention, to be of unlimited duration, will enter into force 180 days after the date of the deposit of the 65th instrument of ratification, but in no case earlier than two years after its opening for signature.

* * *

The 47th UN General Assembly after commending and approving the Convention, requested the Secretary-General, as Depositary of the Convention, to open it for signature at a special conference in Paris, France, on 13 January 1993. By 8 February 1993, 137 States had signed the Convention.

*Source: UN Chronicle* Vol. XXIX, No. 4. Department of Public Information, United Nations, New York 10017, USA (December 1992).

## *Conservation of Clean Air and Water-Europe*

### *Liquefied petroleum gas*

The oil industry organization, Conservation of Clean Air and Water Europe (CONCAWE), has recently published a report entitled 'Liquefied Petroleum Gas'. It collates the health, safety and environmental data on LPG and its major component streams. LPG consists mainly of propane, butane and isobutane and it may also contain $C_3$ and $C_4$ unsaturated hydrocarbons. Its main use is as a fuel, but it is also in widespread use as an aerosol propellant and as a chemical feedstock. The following is a summary of the report.

#### *Product description*

LPG is predominantly a mixture of $C_3$ and $C_4$ hydrocarbons with other hydrocarbons in the $C_2$-$C_5$ range. These are gases at normal ambient temperatures and pressures. Their liquefaction by application of pressures of a few atmospheres to produce liquefied petroleum gases enables them to be conveniently and efficiently stored and transported in light pressure vessels. Refrigeration to below their boiling point is an economic method of liquefying large quantities of LPGs for bulk storage and transport.

The main constituents of LPGs produced either in petroleum refineries as the light end fractions of distillation and cracking processes, production of crude oil or purification of natural gas are mainly propane and butanes. LPGs produced by secondary refinery processing, e.g. cracking, may contain unsaturated hydrocarbons such as propylene and butenes and small traces of diolefins may

also be produced. Certain specifications permit the presence of up to 10% mol. total dienes in LPG. The level of dienes in LPG is under review and a draft CEN specification for automotive LPGs proposes a maximum level of 0.5% mol. LPGs obtained as the liquid condensate in natural gas or crude oil production (also known as natural gas liquids or NGLs) are less likely to contain appreciable amounts of these unsaturated hydrocarbons.

LPGs normally contain low concentrations of various sulphur compounds. The levels permitted are governed by the technical specification, which typically prescribes limits for total sulphur, hydrogen sulphide, and mercaptans. Depending on the base odour, odourants (also described as stench agents or denaturants) may be added in small quantities (ppm) so that gas leaks may be detected by smell. An anti-icing agent such as methanol may be added in small quantities to prevent ice and hydrate formation in valves or regulators.

LPGs are widely used as fuels and as feedstocks in chemical processes. In some countries there is also extensive use as automotive fuel. A large volume is distributed, much of it in small containers, for domestic heating and cooking use in locations where piped supplies of gas are not available. LPGs are also used as propellants in pressurized aerosol containers.

*Typical properties*

The physical properties of a specific commercial LPG will depend mainly on the relative proportions of propane, isobutane and *n*-butane present and will be intermediate between those of propane and *n*-butane. Most of these properties can be calculated from the content and properties of the major components. Data for these major components of LPGs are shown below.

*Physical properties of the major components of LPG*

| | Propane | Isobutane | *n*-Butane |
|---|---|---|---|
| Boiling point at 101.3 kPa (°C) | −42.1 | −11.8 | −0.5 |
| Liquid density at 15°C (kg/m³) | 506.0 | 561.5 | 583.0 |
| Vapour pressure at 40°C (kPa) | 1510 | 530 | 375 |
| Flash point (°C) | −104 | −107 | −60 |
| Upper explosive limit (% vol) | 9.5 | 8.5 | 8.5 |
| Lower explosive limit (% vol) | 2.3 | 1.9 | 1.9 |
| Auto-ignition temperature (°C) | 450 | 462 | 405 |
| Vapour volume produced by 1 litre liquid at 15°C, and 101.3 kPa (litres) | 269 | 221 | 235 |
| Vapour density (air = 1) | 1.551 | 2.07 | 2.07 |

*Toxicity*

There are no reports in the published literature of toxicity studies on LPGs. However, information published on the major components, propane and butane is useful for predicting the likely toxicity of LPG. It should be noted that propane and butane at sufficiently high concentration are anaesthetics and some effects reported are a manifestation of their anaesthetic properties.

*Propane.* Propane gas is an anaesthetic and is non-irritant to the skin and eyes. Direct contact with liquefied propane causes burns and frostbite. Exposure of cats by inhalation to 89% (% vol. in air) showed decreased blood pressure but this was below the anaesthetic concentration. Guinea pigs exposed to atmospheric concentrations between 2.2 and 5.5% vol. showed 'sniffing and chewing movement' but these effects were rapidly reversible on cessation of exposure.

In rhesus monkeys, a depressed breathing rate was the only effect observed from 15-minute exposures to 100,000 up to 200,000 ppm (10 to 20%). Blood pressure changes were reported in dogs after exposure to 25,000 ppm (2.5%). Effects on blood pressure, heart stroke rate/volume and pulmonary vascular resistance were reported after exposures to 3.3%. Cardiac sensitization has been reported in dogs at concentrations between 15 and 90% in oxygen and in mice at 10%.

In rats, exposure to 28% for 10 minutes caused CNS depression. The lethal concentration ($LC_{50}$) was greater than 80% following a 15-minute exposure period. The $EC_{50}$ cardiac sensitization to adrenaline in dogs following 5 minutes exposure was 18% vol. Propane gas showed no mutagenic activity when tested in the Ames assay at concentrations up to 50% vol.

*Butane.* In sufficient concentrations, butane gas exhibits anaesthetic properties. The 2-hour inhalation $LC_{50}$ for the mouse has been reported as 286,000 ppm (28.6%) and 4-hour $LC_{50}$ for the rat at 277,000 ppm (27.7%). Butane gas has been reported to be a weak cardiac sensitizer in dogs and guinea pigs at 5,000 ppm (0.5%). The effects were reversible on cessation of exposure. It was found to be non-mutagenic at several concentrations in the Ames test. Butane gas is non-irritant to the eye and skin. Injection into the anterior eye chamber of rabbits did not cause disturbance and the gas disappeared in 2-4 days.

*Unsaturated hydrocarbons (alkenes and dienes).* The lower members of the series (ethylene, propylene and the butylenes) are asphyxiants or weak anaesthetics. Apart from these properties there are no reports on their toxicology in the literature. The anaesthetic potency of the materials increases with their chain length. Ethylene and propylene have been used as surgical anaesthetics.

The toxicology of 1,3-butadiene has been reviewed extensively elsewhere and is not reviewed further in this dossier. The most significant aspect for butadiene is that it has been shown to be carcinogenic in rodents, but there is no direct evidence of its carcinogenicity in man.

*Health hazards*

Under normal conditions of storage and use there is little opportunity for LPGs to present a hazard to health. However, high exposures may result from accidental releases of liquid or vapour. LPGs are heavier than air and, in the event of a leak, vapour may accumulate in confined spaces and low lying areas to present both health and safety hazards.

*Inhalation.* LPG vapour is not a respiratory irritant. Brief exposure to low concentrations does not cause any systemic effects. Inhalation of increasing concentrations (above 10%) will result in narcotic effects such as weakness, headache, light-headiness, nausea, confusion, blurring vision and increasing drowsiness. Exposure to very high concentrations may result in loss of consciousness, convulsions and even asphyxiation as a consequence of oxygen deficiency. The narcotic effect of butane is greater than propane and exposure to a concentration of 1% (10,000 ppm) can cause drowsiness after a few minutes. Although

1,3-butadiene itself may present a chronic health risk after prolonged and/or repeated exposure at the concentrations at which it may be present in LPG, no such health risk is anticipated.

*Ingestion.* Ingestion of LPGs is extremely unlikely to occur under normal conditions because of their physical state.

*Skin and eye contact.* The rapid evaporation of liquid in contact with skin or eyes may produce cold burns. Storage containers and delivery lines may also become cold enough to present a cold burns hazard when LPG is drawn from them (particularly when dealing with propane).

*LPG abuse.* The major hazard associated with the intentional inhalation of LPGs is the risk of sudden death following exposure to high concentrations. Death may occur as a result of simple asphyxia (due to a lack of oxygen in the breathing mixture) or more commonly due to cardiac arrest.

*Exposure limits*

The American Conference of Governmental Industrial Hygienists (ACGIH) has established an 8-hour time-weighted average Threshold Limit Value (TLV-TWA) of 1000 ppm (1800 mg/m$^3$) for LPG vapours. This figure has also been adopted by many countries in national lists of exposure standards. In the UK, a 10-minute TWA limit of 1250 ppm (2250 mg/m$^3$) has also been recommended. An occupational exposure limit of 1000 ppm has been established for propane, butane and isobutane in Germany. An 8-hour maximum exposure limit of 10 ppm (22 mg/m$^3$) has been established for 1,3-butadiene in the UK. In Germany, a TRK value (Technical Guiding Concentration) of 15 ppm has been established for loading or polymerization processes involving 1,3-butadiene. For other operations, involving exposure to butadiene, the TRK value for an 8-hour day is reduced to 5 ppm.

*Safe handling advice*

The principle hazards associated with LPGs are their extreme flammability.

Personnel who handle or use LPGs should be informed of the potential hazards and the necessary safe handling procedures and precautions. A standard practice has been described for safe sampling of LPG. It should be noted that due to their low boiling points LPGs can cause cold burns. Propane (boiling point $-42$°C) presents a greater hazard than the butanes. When handling LPG the following are important:

—Inhalation of LPG vapours should be minimized. If there is a risk of exposure to high vapour concentrations respiratory protection/breathing apparatus should be worn.

—Contact with liquid and with containers or delivery lines from which LPG has just been drawn, should be avoided by use of suitable protective clothing, to prevent cold burns.

—If there is a risk of eye contact when handling the liquid, suitable eye protection such as goggles and/or face shield should be used.

—LPG is an effective solvent of petroleum and rubber products. Care should be taken when selecting the appropriate handling material to ensure that they are compatible with LPG and will not adversely deteriorate under operating conditions.

—Clothing which has had liquid LPG spilt on it should be removed as soon as possible. The liquid could be trapped in the fibres; complete evaporation may be delayed, for example, until the wearer enters a warm room, giving rise to a fire hazard.

—In the event of a liquid spillage, efforts should be made, for example with water fog sprays, to direct the flow of vapour to a safe location. Because of fire and explosion hazards, persons should be evacuated and not be allowed to re-enter the area until it has been declared safe by a competent person. The possible accumulation of potentially explosive/flammable atmospheres and of high concentrations which could lead to asphyxiation, occurring in confined spaces or low lying areas, must be recognized.

—In cylinder-filling operations the wearing of impervious gloves, overalls or apron and face shield and/or goggles is advisable. Protective footwear should be worn when handling cylinders. Hearing protection may also need to be worn.

—LPG should be stored outdoors or in adequately ventilated storerooms. Where cylinders are used indoors, for example with space heaters, it is recommended that only the cylinder in use be kept inside the building. Sources of ignition should be kept well away from LPG cylinders in storage.

—LPG cylinders should not be stored in the vicinity of cylinders containing compressed oxygen.

—Emergency response plans should be developed for each depot and filling plant.

*Emergency treatment*

*Inhalation.* Remove the casualty to fresh air, taking all appropriate steps to avoid fire, explosion and inhalation hazards to the rescuers. Precautions may include the use of breathing apparatus. Keep casualty at rest and warm. (N.B. If the casualty is stuporous, some physical restraint may be necessary to prevent injury.) If unconscious, place in the recovery position and give oxygen if available. Monitor breathing and pulse; if necessary, assist respiration, preferably by an exhaled air method and give external cardiac massage. Obtain medical assistance urgently.

*Skin contact.* In case of contact with liquid, drench affected parts with water. Remove contaminated clothing, rings and watches etc. if possible, but *do not* attempt to do so if these are adhering to the skin. Do not make any attempt to reheat rapidly. *Slowly* reheat the affected part.

*Eye contact.* In the case of liquid contact, immediately flush the eyes with copious amounts of water for up to 15 minutes. Cover the eye with a sterile dressing. Seek medical attention immediately.

*Information for doctors.* No specific treatment is indicated. Supportive measures appropriate to the patient's condition should be provided.

*Disposal*

The need to dispose of LPG seldom arises for the following reasons:

—LPG is highly volatile under normal ambient temperature and pressure conditions.

—End uses for LPGs result in: (i) combustion, when used as fuels; (ii) incorporation into other chemical struc-

tures, when used as chemical feedstock; (iii) dispersion into the atmosphere, when used as aerosol propellants.

No specific recommendations regarding disposal other than the avoidance of uncontrolled combustion are necessary.

*Fire and explosion hazards*

Fire and explosion are the main LPG hazards. The flash point is below −40°C. Explosivity limits are approximately 1.9 to 9.5% by volume in air. Apart from use as fuel under controlled conditions, sources of ignition should be kept well away from LPG.

Small fires should be extinguished with dry powder. Large fires should only be fought by properly trained firefighters. Any containers subject to fire or to radiated heat should be cooled by water application, this is probably important in the case of containers of pressurized or liquefied gases. Water fog should be used to assist approach to the source of the fire. All areas where there is significant storage of LPG should be fitted with an automatic fire fighting system. Furthermore, management at such locations should have prepared emergency and disaster plans in conjunction with local authorities.

The liquid has a marked tendency to build up a static charge when transferred by pipelines and it is essential to earth receiving and transfer vessels as well as the pipelines.

*Environmental hazards*

An extensive search of the literature failed to identify any references to the ecotoxicological effects of LPG or its primary constituents. Because of their high volatility, LPGs are unlikely to cause ground or water pollution. LPGs released into the environment will rapidly disperse into the atmosphere where they will undergo photochemical degradation.

*Source:* Liquefied Petroleum Gas. CONCAWE Report No. 92/102. Brussels (June 1992).

## Germany

### Reports on chemicals of environmental relevance

The Advisory Committee on Existing Chemicals of Environmental Relevance, for short, BUA (Beratergremium für umweltrelevante Altstoffe), was established by the German Chemical Society (Gesellschaft Deutscher Chemiker) in 1982 in collaboration with the Federal Government, the scientific community and the chemical industry. It was unanimously accepted that the incorporation of the committee into an internationally recognized scientific society offered the guarantee of relevant research conducted according to scientific principles. The compilation of environmentally relevant chemicals is a considerable task. Therefore, it is not surprising that in the beginning BUA first had to find sensible and justifiable means of solving this task. This resulted in the publication of an expanding series of Reports on Chemicals of Environmental Relevance that are designed to indicate ways and means to deal with the problems associated with existing chemicals. The committee have selected the environmentally most important substances from an estimated 100,000 chemicals currently on the European Community market. These chemicals are examined according to eight criteria covering environmental exposure and effects (e.g. occurrence and degradability in water and air, bioaccumulation, toxicity, mutagenic or carcinogenic characteristics).

Part I of the reports presents the criteria for evaluating the environmental significance and toxicity of chemicals and lists 60 chemicals of particular environmental relevance. Part II expands the original list of chemicals to include a further 75 substances and provides additional criteria for their selection (e.g. production volume of each chemical).

The bulk of the series comprises in-depth considerations of individual chemicals, providing comprehensive information on the possible hazards of the chemicals to health and the environment. Each report is structured clearly and provides the following data:

—chemical and physical characteristics
—analytical chemistry
—emission into the environment during production processing, applications, and waste disposal
—occurrence in the environment
—behaviour in the environment
—ecotoxicology
—toxicity in warm-blooded animals
—substance-specific legal regulations
—summary and conclusions
—recommendations
—references.

Readers will find the report on bis(2-chloroethyl) ether summarized in this Bulletin in Section III 'News about Chemicals' page 24.

Inquiries and copies of these reports are available on request from: Gesellschaft Deutscher Chemiker, P.O. Box 101161, D-6940 Weinheim, Federal Republic of Germany.

## Netherlands

### Risks of dangerous substances exported to developing countries

In February 1992 the Health Council of the Netherlands published a report on the risks of dangerous substances exported to developing countries. The Committee which prepared this report concluded that even if the Prior Informed Consent (PIC) procedure included in the London Guidelines for the Exchange of Information on Chemicals in International Trade and the International Code of Conduct on the Distribution and Use of Pesticides is enforced along the lines proposed by the Committee, it would not in itself be enough to prevent dangerous situations occurring from the use of hazardous substances in certain developing countries. The following is an executive summary of the report.

The use of hazardous substances is no longer confined to industrialized countries. In developing countries, too, there has been a considerable growth in the use of pesticides and industrial chemicals over the past few decades. Many of these substances are imported from industrialized countries.

The use of chemicals entails risks for human health and ecosystems. There are strong indications that they can cause particularly serious problems in developing countries. Industrialized countries have now become aware that exporting hazardous substances to developing countries entails

certain responsibilities. Realizing this, the Dutch Minister and State Secretary for Welfare, Health and Cultural Affairs and the Minister for Housing, Physical Planning and Environment asked the Health Council of the Netherlands for advice on the risks of hazardous substances that are exported to these countries. The members of Government asked, among other things, to what extent Dutch risk evaluation methods are applicable to chemicals intended for use in developing countries. They also enquired about suitable risk-limiting measures which could be taken by the exporting country. In this advisory report an *ad hoc* committee of the Health Council addresses these questions.

The committee points out first of all that the final responsibility and the choice of whether or not to import hazardous substances are in principle a matter for the authorities in the developing countries concerned. However, industrialized countries are obliged to provide those authorities with the knowledge and means necessary for proper risk evaluation and control, along with products and equipment which are also safe to use in high-risk situations.

The committee performed a rough analysis of the problems concerning the use of hazardous substances (both pesticides and industrial chemicals) in the Third World. It concluded that the literature on the nature and extent of these problems is limited. Analysis is also hampered by the fact that there are great local and regional economic, ecological, agricultural, social and political differences between developing countries. These differences imply that the risks posed by hazardous substances are not the same in all developing countries. Nevertheless, the committee believes that a number of generally valid factors can be identified which contribute to an increased risk from the use of such substances in the Third World. The most important of these are:

—excessive use or misuse of substances
—use of acutely toxic substances without adequate safety measures
—failure to use protective clothing (e.g. because of the climate)
—lack of care when transporting or handling substances
—poor information provisions, leading to a lack of knowledge about the risks involved
—use of cheap, often more dangerous substances and faulty equipment
—inadequate management and storage of obsolete stocks and used packaging materials
—lack of facilities for waste processing
—lack of legislation on working conditions and lack of monitoring pollutants in the (working) environment and in food
—easy access to acutely toxic substances (suicide)

The committee is also aware that in industrialized countries compliance with legislation and safety regulations for hazardous substances leaves much to be desired. Therefore, not all of the problems outlined in its report are confined to developing countries.

In an (eco)toxicological risk evaluation, data on the toxicity of a substance are combined with figures on the expected concentrations of that substance in the environmental compartment or foodstuff in question (exposure). From its evaluation of the problems caused by hazardous substances in the Third World, the committee concludes that the risks to humans and ecosystems there differ from those in industrialized countries mainly as a result of differences at the exposure stage. The extent of exposure and the chance of abnormal or increased exposure to hazardous substances are greater in developing countries. Hazardous situations may arise anywhere along the route of a substance in a country (production, sale, transport, storage, use and waste processing). Differences in the toxicity of a substance, caused among other things by differences in the sensitivity of organisms and ecosystems and variations in environmental conditions, will not, in many cases, constitute the main cause of the difference in risk.

The committee therefore assumes that risk evaluation of substances intended for use in the Third World can be based on the methods and results of risk evaluations for industrialized countries. However, a specific analysis of possible differences in distribution and exposure in the recipient country must also be performed. In the opinion of the committee, extra attention should be given to patterns in use, to the method and site of application and the behaviour of the substance in that country. This report contains a systematic checklist to be used by policy makers in developing countries for identifying differences in exposure to a substance and estimating the risks.

In the opinion of the committee, effective protection of ecosystems in developing countries is impossible without an extensive ecotoxicological study of the harmful effects of chemicals on those ecosystems. The committee assumes that, generally speaking, the functional groups of organisms exposed to hazardous substances are the same in both tropical regions and temperate zones. Ecotoxicological risk evaluation would be improved, however, if more native specimens of these functional groups were involved in the (prior) toxicological studies.

Extra information of this kind regarding the sensitivity of organisms and ecosystems in the Third World will lead to a more balanced risk evaluation even though, as has been pointed out, better information on local exposure levels is more important. In this connection the committee feels that more research should be done into the influence of a poor human health status (such as reduced liver function as a result of malnutrition) on the toxic effects of substances.

The realization that exporting countries are also responsible for the risks posed by hazardous substances in importing countries has led, among other factors, to the international adoption of the principle of 'prior informed consent' (PIC). According to this principle the export of a substance which is banned or severely restricted in the exporting country and which is included in the international PIC list may not proceed without the agreement of the relevant authority in the importing country. The question now is whether other substances, which are not included in the PIC list, might also cause serious problems when used in developing countries. The members of Government therefore asked the Health Council to examine what further health and environmental criteria the Government could employ when selecting PIC substances in the light of a possible export to Third World countries.

Evaluations of problems with chemicals indicate that, in the Third World, substances with high dermal or respiratory toxicity pose particular risks to humans. One of the main reasons for this lies in the fact that protective measures simply cannot be taken or, when taken, are ineffective. Several acutely toxic chemicals are not forbidden or

severely restricted and thus they will not be included in the international PIC list. The committee therefore recommends that all acutely toxic substances which meet the criteria for inclusion in classes 1A and 1B of the WHO list (extremely and highly hazardous chemicals) be included in the PIC list. It also recommends inclusion of acutely toxic volatile substances.

In addition, the committee does not exclude the possibility that substances which only produce effects after long-term exposure may cause at least equal damage to human health in developing countries as acutely toxic substances. No data are available on this because chronic poisoning is more difficult to identify than acute poisoning. However, there is a good chance that exposure to chronically toxic substances is also greater in developing countries than in industrialized countries. The reasons for this are virtually the same as those behind the greater exposure to acutely toxic chemicals, and include the lack, inadequacy or incorrect application of safety measures. According to the committee, too little is known at present to be able to identify one or more chronic toxicity criteria that could be strictly adhered to when selecting substances for the PIC list. However, it stresses the need for more attention to the risks of long-term exposure in developing countries.

With regard to the protection of ecosystems, the committee believes that at the moment it is virtually impossible to say whether the export of hazardous substances to the Third World should be subject to generally applicable ecotoxicological criteria and if so, what those criteria should be. One problem lies in the fact that the differing environmental conditions in those countries affect the factors which determine the risk in very different ways. The ecological risk posed by chemicals is in fact determined by a combination of factors. Furthermore, the current gaps in knowledge and the wide variations in environmental conditions and in ecosystems only serve to increase the uncertainty. The committee believes that, in general, in Third World countries there is a strong possibility that large quantities of pollutants will end up in surface waters. It therefore believes that more attention should be given to substances which are acutely toxic for aquatic organisms.

The committee believes that even if the PIC procedure is enforced, it would not in itself be enough to prevent dangerous situations occurring with hazardous substances in the Third World. A combination of preventive measures is needed if the risks are to be limited. In its report, the committee examines a number of possible measures and indicates where the possibilities and responsibilities lie. Particular attention is given to the promotion of integrated pest management and cleaner technologies, improvement of the quality and safety of the product and the equipment used in its application. Emphasis is also placed on what information is needed, improvement of the exchange of information about substances and training in ways of handling information and in a safe use of chemicals. As far as the provision of information is concerned, the committee believes that the various international organizations should ensure that their channels of information are more effectively focused on the target groups and that they are better coordinated with each other. Collaborative efforts should be taken by governments, industry and non-governmental organizations not only to improve the information exchange, but also to promote awareness of the hazards and ensure that safe products and equipment are used.

Finally, the committee highlights the dilemma posed by the fact that, while it should be left to a country to decide whether it wants to import a particular substance, experience has taught that certain substances always create risks in developing countries. There is also a category of substances (including DDT, asbestos and CFCs) which cause problems all over the world. In the opinion of the committee, a worldwide campaign should be conducted against the use of these substances.

*Source:* Report on the Risks of Dangerous Substances Exported to Developing Countries. Gezondheidsraad, Health Council of the Netherlands, Postbus 90517, 2509 LM Den Haag, Netherlands (1992). Report in Dutch with an Executive Summary in English.

## *Sweden*

### *Principles for identifying unacceptable pesticides*

The Swedish National Chemicals Inspectorate (KEMI) published recently a report on the principles for identifying unacceptable pesticides. The purpose of the report is to describe when the Swedish National Chemical Inspectorate considers a pesticide to be unacceptable from a health and environmental protection standpoint on the basis of its intrinsic properties. These principles and guidelines are also meant to facilitate a uniform and efficient handling of applications for approval.

Pesticides may not be imported, offered for sale, transferred or used without being approved by the Chemicals Inspectorate. Under the provisions of Section 5 in the Ordinance (SFS 1985:836) on Pesticides, a pesticide may be approved only if it is acceptable from the standpoint of health and environment protection. This report reflects the view of the Chemicals Inspectorate on these matters.

The risk of harmful effects on human health and the environment is dependent on the exposure as well as the intrinsic properties of a chemical substance or preparation. The report presents a set of general principles for identifying clearly unwanted properties in pesticides. However, in order to establish if a pesticide with clearly unwanted properties is unacceptable it is also necessary to perform an exposure assessment. The guidelines for identifying unacceptable pesticides presented here are therefore based both on intrinsic properties and exposure. It is, however, beyond the scope of this report to describe how to interpret the result of the exposure assessment. Because of the wide variety of different exposure situations this assessment should be made on a case-by-case basis. Pesticides with clearly unwanted properties which may—at potential levels of exposure—give rise to unacceptable risks will not be approved.

Some older pesticides that may present unacceptable risks still remain on the market. The guidelines are also meant to serve as a basis for the assessment of these pesticides. Pesticides regarded as unacceptable will be removed from the market or severely restricted. Certain pesticides have particularly serious properties. The qualitative and quantitative limits for such intrinsic properties are here called cut-off criteria. Pesticides which fulfil the cut-off criteria are regarded as unacceptable within the meaning of the Ordinance solely on the basis of their intrinsic properties. These pesticides will be removed from the market promptly or with a short phase-out. The cut-off criteria are set with a sufficient margin so that in the case of non-approval there

should be no doubt of the decision being the same after a risk assessment which takes the exposure into consideration.

Exposure to man and the environment varies to a great extent between differing handling situations. The following cut-off criteria therefore refer only to pesticides used in agriculture and areas of use with similar handling situations. Within these areas, exposure conditions may also vary widely. An exemption from the cut-off criteria may therefore be justified if for a specific use of a pesticide it can be shown that exposure of humans and the environment in possible handling situations is very low.

In this report pesticides classified in categories very toxic, toxic or highly corrosive are regarded as having clearly unwanted or particularly serious properties.

Even if a pesticide is not regarded as unacceptable according to these guidelines or cut-off criteria it may still be regarded as unacceptable after a risk assessment which takes all hazardous properties into consideration. Furthermore, according to the principle of substitution in the Swedish Act on Chemical Products, a pesticide should not be approved if there are better alternatives from the standpoint of health and environmental protection.

*Source:* Principles for Identifying Unacceptable Pesticides. Report No. 4/92. Swedish National Chemicals Inspectorate (KEMI), P.O. Box 1384, S-171 27 Solna, Sweden (1992).

## *United States*

### *Analysis of risk that granular pesticides pose to birds*

On 28 May 1992, the United States Environmental Protection Agency (EPA) released an analysis comparing the risk to birds posed by different granular pesticides and announced plans to use a new approach to evaluate further those chemicals posing the highest risk.

Pesticides in the form of dry granules pose a particular risk to birds foraging in treated fields since the granules can be consumed by birds as grit or with food elements.

EPA's analysis identified 14 compounds—out of the universe of 99 granular pesticides—that the Agency believed may pose a high risk of killing birds. The 'Comparative Analysis of Acute Avian Risk from Granular Pesticides' does not constitute a regulatory action, but is simply a tool for screening avian risk from granular pesticides. Because these compounds pose a similar risk to birds, before proceeding with regulatory action on any one chemical, EPA decided to use a cluster approach—an alternative to the chemical-by-chemical analysis— to evaluate further many of these 14 pesticides together with the other pest control alternatives used on specific sites. The two sites selected for the cluster projects are corn at planting time and turf (including home lawns).

'EPA's goal in analysing the risks and benefits of granular pesticides in clusters is to end up with those compounds on the market which pose the least amount of risk to birds and other wildlife while promoting consideration of non-chemical alternatives' said Linda Fisher, EPA's Assistant Administrator for Prevention, Pesticides and Toxic Substances. 'We believe that this approach will ultimately provide the greatest safeguard for birds and wildlife, will be the most equitable way to evaluate the granular pesticides and cause the least disruption to growers.'

In the analysis, EPA evaluated both the inherent toxicity of granular pesticide products and the exposure birds may have to these pesticides, given actual use patterns at different sites. In characterizing the avian risks, EPA also looked at incident reports of bird kills and field studies showing bird mortality.

Of the 99 granular pesticides examined in the comparative analysis, 85 were eliminated either because they were not highly toxic to birds or because they were used in such a manner that birds had only limited exposure to them. The remaining 14 granular pesticides, all of which are carbamate or organophosphate insecticides, are the following: aldicarb, bendiocarb, carbofuran, chlorpyrifos, diazinon, disulfoton, ethoprop, ethyl parathion, fenamiphos, fonofos, isofenphos, methomyl, phorate, and terbufos.

The cluster approach will focus on corn at planting time and turf, selected on the basis of high pesticide use and potential for risk reduction. All but one of the pesticides of concern are registered for use on either corn or turf.

Corn production is the single largest use of granular pesticides – more than 20 million acres are treated annually. About 2.5 million acres of turf are treated annually with granular formulation pesticides. EPA believes that both sites offer potential for risk reduction through the use of alternative pest-control technologies involving safer pesticides, reduced chemical use, or non-chemical strategies. EPA's cluster projects will evaluate other environmental and human risks and will include formulations other than granular.

Before beginning the cluster reviews, EPA is allowing registrants of the 14 pesticides identified in the analysis 90 days to propose voluntary risk reduction measures, such as lower application rates, fewer applications per year, and better soil incorporation. The Agency is encouraging registrants to amend their labels now in order to realize some immediate reductions in the amount and availability of these toxins in the habitat of birds and other wildlife.

EPA has already taken regulatory action on two of the pesticides based on risk to birds. The use of diazinon, both liquid and granular, has been cancelled on golf courses and sod farms and the Agency has reached an agreement with the registrant of carbofuran to phase out more than 99% of the use of the granular formulation of this chemical by 1994. EPA has also proposed regulatory action on aldicarb based on groundwater risk. Further, EPA has reached an agreement with the registrants of ethyl parathion to cancel most uses due to worker risk. This cancellation includes all granular uses of ethyl parathion.

*Source:* Copies of the 'Comparative Analysis of Acute Avian Risk from Granular Pesticides', a fact sheet, and other materials are available by writing to the Public Response and Programme Resources Branch, Field Operations Division (H7506C), Office of Pesticide Programmes, U.S. EPA, 401 M Str., S.W., Washington, D.C. 20460, United States (28 May 1992).

# III. News about chemicals

## Bis(2-chloroethyl)ether

The Society of German Chemists (GDCh) and the Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) published a report on bis(2-chloroethyl)ether. A summary of this report is given below.

**Identity**

| | |
|---|---|
| *Common name:* | Bis(2-chloroethyl)ether |
| *Chemical names:* | |
| IUPAC | Bis(2-chloroethyl)ether |
| CAS | Ethane, 1,1-oxybis(2-chloro-) |
| *Common trade names:* | Bis(2-chloroethyl)ether (BCEE); 2,2'-Dichloroethyl ether; 1-Chloro-2(β-chloroethoxy) ethane; Dichloroethyl oxide; Sym. Dichloroethyl ether; Chlorex; β,β'-dichloroethyl ether |
| *Chemical structure:* | $Cl\text{-}CH_2\text{-}CH_2 - O\text{-}CH_2\text{-}CH_2\text{-}Cl$ |
| *Molecular formula:* | $C_4H_8Cl_2O$ |
| *Registry numbers:* | |
| CAS | 111-44-4 |
| EC | 603-029-2 |
| RTECS | KN 0875000 |

*Some physical and chemical properties*

| | |
|---|---|
| *Boiling point (1013 hPa):* | 178°C |
| *Melting point:* | – 50°C |
| *Density (20°C):* | 1.22 g/cm³ |
| *Vapour pressure (20°C):* | 0.933 hPa |
| *Flash point:* | 55°C |
| *Ignition temperature:* | 365°C |
| *Refraction index ($n_{D^{20}}$):* | 1.457 |
| *Viscosity (25°C):* | 2.065 mPa.s |
| *Water solubility (20°C):* | 10,200 mg/l |
| *n-Octanol/water partition coefficient (log $P_{ow}$):* | 1.26<br>1.58 |

Bis(2-chloroethyl)ether (BCEE) is a colourless and clear liquid which smells like chloroform and irritates the eyes and mucous membranes. The ether is miscible with most organic solvents in addition to the paraffin hydrocarbons.

BCEE is not hydrolysed at temperatures under 100°C despite its easily activated chlorine atoms located in the 2-position to oxygen. A step-wise substitution or cleavage of the chlorine atoms first occurs under more drastic conditions. 2-Chloroethylvinyl ether and dioxane are formed as main products from heating with NaOH to 200-220°C. At 200°C the corresponding N-arylmorpholines with aniline or other primary aromatic amines is obtained. BCEE has been used to synthesize macrocyclic polyethers (crown ethers).

*Analysis*

Because BCEE is present in the environment in small concentrations, enrichment procedures are necessary in order to analyse it. Columns with activated charcoal, silica gel or adsorbent resins can be used to enrich BCEE from water. In order to isolate it from aqueous or solid samples, extraction with organic solvents, preferably with hexane, can be employed. BCEE can be evaporated from aqueous samples because of its relatively high volatility and can be separated from the matrix and enriched according to static and dynamic vapour-chamber analytical techniques. Depending on the applied technique, enrichment factors ranging from 10 to 1000 can be attained.

Gas chromatography is best suited for the determination of BCEE from environmental samples. The separation of BCEE from other sample constituents is guaranteed through suitable separation columns selected according to the matrix and accompanying components. The following detectors can be applied: flame ionization detector (FID); electron capture detector (ECD); electrolyte-conductivity detector (HALL detector); and a mass spectrometric detector (MS). Because the detection limits of these detectors range from a few nanograms (FID) to ca. 100 picograms (MS), the detection limit attained thus depends on the enrichment step of the sample preparation. Detector selectivity, which determines the extent to which BCEE is differentiated from the other sample components, is also significant. Selectivity increases in the order: FID, ECD, HALL and MS. Detection limits of BCEE in environmental samples in the nanogram range can be attained by applying corresponding enrichment techniques and selective detection principles.

*Ecological aspects*

*Occurrence and compartment distribution.* Up to the mid-1960s, bis(2-chloroethyl)ether (BCEE) was a by-product of the production of ethylene oxide by the chlorohydrin process amounting to 5-9% by weight of the ethylene oxide produced. The by-product was used industrially. After the chlorohydrin process was discontinued, specific production of BCEE was continued; however, today BCEE is neither produced specifically nor is it a by-product of any process in Germany. In accordance to these facts, despite improvements in analytical methods, BCEE has not been detected in water samples taken from the River Rhine in Germany and the Netherlands. There is no information available on detection in soil and organisms in Europe.

*Degradability and bioaccumulation.* There is hardly any literature on the microbial degradation of BCEE. Under the conditions of the closed bottle test, complete mineral-

ization of the compound was found after 7 days without adaption. In a seepage test with rapid passage through the soil no degradation was observed. The accumulation of BCEE by fish is only very slight (a factor of 11). The tissue concentration decreases again within a few days.

*Ecotoxic effects.* The toxic effects, determined as the $EC_{50}$ (48 h) of BCEE on the water flea *Daphnia magna* and tested in a closed system because of the expected volatility of the substance, was found to be of the order of 300 mg/l. The $EC_{50}$ in an acute test on fish (*Lepomis macrochirus*) was reported as 600 mg/l after exposure for 96 hours. No other quantitative ecotoxicological data are available.

*Toxicological aspects*

BCEE is categorized as toxic under the provisions of the Chemical Act (Section 3.3). The substance is a potent irritant for the respiratory system and mucosa. Although only slightly irritant to the skin, toxic effects may occur due to the efficient dermal absorption. The compound and its metabolite chloroacetaldehyde are expected to have cytotoxic effects because they are able to cross membranes and are reactive. Genotoxic effects have been found only in the *in vitro* test systems. Because of the analogy to vinyl chloride – which also forms chloroacetaldehyde as a metabolite in addition to chlorooxirane, whose genotoxic potential was recognized only later – the possibility of carcinogenicity was suggested. However, in contrast to vinyl chloride, this is at the most very slight. Since further investigations have shown that the carcinogenic effect of vinyl chloride derives from the epoxide chlorooxirane and not from the metabolite which is common to vinyl chloride and BCEE, i.e., chloroacetaldehyde, the suspicion for a carcinogenic effect was ruled out. The Deutsche Forschungsgemeinschaft (German Research Council) Commission for the investigation of health hazards of chemical compounds in the work area removed BCEE from Group III B of the MAC list in 1984. The MAC was set at 10 ppm.

*Recommendation*

BCEE is no longer produced in the Federal Republic of Germany or Central Europe, nor does it occur as a by-product. Furthermore BCEE has not been detected in recent samples of the environment. Consequently, the ecotoxicological risk is estimated to be low. Hence there is no need at present for further investigations. However, if BCEE does appear in future, it should be pointed out that there are still gaps in our knowledge concerning the sensitizing potential and the reproduction toxicology of BCEE and also for the ecotoxicological behaviour.

*A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case Postale 356, 15 Chemin des Anémones, CH-1219 Châtelaine, Geneva, Switzerland.*

*Source:* Bis(2-chloroethyl)ether, BUA Report No. 21. VC H Verlagsgesellschaft, P.O. Box 101161, D-6940 Weinheim, Federal Republic of Germany (1992).

## *1,2-dibromo-3-chloropropane*

The KEMI report 'Effects on Reproduction of Chloroform and 1,2-dibromo-3-chloropropane' published by The Swedish National Chemicals Inspectorate, results from a project, established by the Nordic Control Group under the Nordic Council of Ministers, to provide an evaluation on the reproductive hazards of different chemical compounds based on current knowledge. The following summary deals with the effects on reproduction of 1,2-dibromo-3-chloropropane (DBCP).

| **Identity** | |
|---|---|
| *Common name:* | Dibromochloropropane |
| *Chemical name:* CAS | 1,2-dibromo-3-chloropropane |
| *Synonyms and trade names:* | DBCP, dibromochloropropane, dibrom-chlorpropan, Fugagon, Fumazone, Nemagon, Nemanax, Nematox |
| *Chemical structure:* | $CH_2Br$-$CHBr$-$CH_2Cl$ |
| *Molecular formula:* | $C_3H_5Br_2Cl$ |
| *Registry numbers:* | |
| CAS | 96-12-8 |
| RTECS | TX 8750000 |

| *Physical and chemical properties* | |
|---|---|
| *Physical state:* | brown liquid |
| *Melting point:* | 6.7°C |
| *Boiling point:* | 196°C |
| *Vapour pressure:* | 0.8 mmHg at 21°C |
| *Flash point:* | 82°C |
| *Solubility:* | slightly soluble in water; miscible with hydrocarbons, ethanol, methanol, isopropanol and halogenated hydrocarbons |
| *Conversion factor at 25°C:* | 1 ppm = 10 mg/m³<br>1 mg/m³ = 0.1 ppm |

*Use and exposure*

DBCP is produced by the addition of bromine to allylchloride. In 1974, production was at least 40,000 tonnes. At that time DBCP was used as a soil fumigant for control of nematodes. However, this use has ceased due to the carcinogenic and reproductive effects of DBCP. DBCP may be used in the chemical and pharmaceutical industry as a raw material for organic syntheses. In the flame retardant tris(2,3-dibromopropyl)phosphate DBCP can be found at concentration levels of 0.002% to 0.05%.

In a manufacturing plant average exposure levels of 4 mg/m³ (0.4 ppm) DBCP have been found. For pesticide applicators exposure levels in the range of 8 to 53 ppb have been recorded. Present day exposure to DBCP is very limited due to the restricted use of the chemical, such as in the chemical and pharmaceutical industry and in some research laboratories.

*Acute toxicity*

*Human data.* No human data on the acute toxicity of DBCP have been found.

*Animal data.* DBCP has moderate acute toxicity in animals as shown in the following table.

| | Species | Route | Value |
|---|---|---|---|
| $LD_{50}$ | Rat | oral | 150-620 mg/kg |
| $LD_{50}$ | Rat | oral | 170 mg/kg |
| $LD_{50}$ | Mice | oral | 257 mg/kg |
| $LD_{50}$ | Rabbit | oral | 180 mg/kg |
| $LD_{50}$ | Guinea pig | oral | 150-300 mg/kg |
| $LD_{50}$ | Rabbit | percutaneous | 1400 mg/kg |
| $LC_{50}$ | Rat | inhalation 8h | 103 ppm |

In single exposures irritation of the eyes and respiratory tract was observed in rats inhaling concentrations of 60 ppm DBCP or higher. Liquid DBCP caused irritation of the skin and the eyes in rabbits. A single subcutaneous dose of 40 mg/kg body weight given to F344 male rats caused histopathological changes of the kidneys, liver, and testes.

*Chronic toxicity*

*Human data.* Except for reproductive effects (see below) no human data on the chronic toxicity of DBCP have been found.

*Animal data.* Liver, testes, and kidney necroses have been observed in male F344 rats after four daily subcutaneous doses of 40 mg DBCP/kg body weight. It has been stated that DBCP is known to induce liver and kidney necrosis, testicular atrophy, stomach cancer, and dominant lethality in some experimental animals.

*Toxicokinetics*

The main route of DBCP uptake is via inhalation. It can also be taken up via the skin and the gastrointestinal tract in humans as well as in animals. Earlier studies have shown that DBCP is metabolized to epichlorohydrin, alphachlorohydrin, and oxalic acid. These metabolites are excreted in the urine as mercapturic acids after conjugation with glutathione.

There are large interspecies variations concerning the ability of DBCP to lead to hepatic, renal, and testicular toxicity. These interspecies variations appear to be closely related to differences in toxicokinetics. In a study of the potential of DBCP to elicit renal necrosis it was observed that single intraperitoneal injections in Wistar rats caused renal necrosis, whereas mice, hamsters and guinea pigs were clearly less sensitive. Earlier kinetic studies have shown that DBCP is rapidly absorbed following i.p. administration, and that it concentrates in the kidney. Following i.p. administration of DBCP (85 μmol/kg), the concentration of DBCP in plasma, liver and kidney was determined after 20 min. to 8 h. Renal and hepatic levels of DBCP were higher than the plasma concentrations at all time points in the four species. After 20 min., substantially higher levels of DBCP were measured in the plasma, liver, and kidney of rats and guinea pigs compared to the respective levels in mouse and hamster. DBCP was eliminated much more rapidly from the mouse, hamster, and guinea pig kidney than from the rat kidney. The renal tissue concentration remained much higher in the rat than in the other species. Furthermore, the higher rates of liver microsomal metabolism of DBCP by mouse and hamster compared to the rat may contribute to the low kidney levels of DBCP in these two species.

Metabolism of DBCP appears to be a necessary step in the pathogenesis of organ damage. DBCP may be activated to reactive metabolites both by a P-450 and a glutathione (GSH) S-transferase pathway. Oxidative metabolism by P-450 seems to be responsible for the mutagenic activity of DBCP in bacteria, but appears to be of minor importance in causing toxicity in mammalian cells. Halogenated alkanes may be activated to reactive episulfonium metabolites by conjugation with GSH. Recent data indicates that DBCP-induced testicular DNA damage may also be mediated by GSH conjugation.

*Mutagenicity*

DBCP has been found mutagenic in *Salmonella typhimurium* TA100, TA1530, TA1535, but not in TA1538, both in the presence and absence of S9-mix. It has been found positive in the sex-linked recessive lethal test using *Drosophila melanogaster*.

In Chinese hamster V79 cells, DBCP caused an increased frequency of sister cromatid exchange indicating that the DNA single strand breaks induced by DBCP may develop into more permanent DNA damage. In male rats DBCP is an inducer of dominant lethal mutations, and in male mice it has not been shown to induce dominant lethal mutations but it has been positive in the mouse spot test.

*Carcinogenicity*

The National Cancer Institute has investigated the carcinogenicity of DBCP using gavage studies in mice (110 or 215 mg DBCP/kg bw) and in rats (15 or 29 mg DBCP/kg bw). In both sexes of both species highly increased frequencies of carcinomas of the forestomach were found.

The International Agency for Research on Cancer has concluded that there is sufficient evidence that DBCP is carcinogenic in mice and rats, and regards DBCP as if it presents a carcinogenic risk to humans.

*Evaluation*

*Toxicokinetics.* 1,2-dibromo-3-chloropropane is known to pass into foetal blood of rats.

*Endocrine and gonadal function.* Several human studies have shown that DBCP affects spermatogenesis. Prolonged occupational exposures have resulted in increased frequencies of azoospermia and oligospermia. Secondary to the effect on spermatogenesis, increased serum levels of follicle stimulating hormone and luteinizing hormone are obtained.

*Fertility.* Fertility of male rats and rabbits has been affected after inhalation of 10 ppm 6 hours/day 5 days/week for 8 weeks.

*Pregnancy and lactation.* The direct exposure of field applicators to DBCP appears to be associated with risk of spontaneous abortion in their wives. In mice DBCP does not seem to be foetotoxic or teratogenic at doses not toxic to the mother.

*Concluding remarks*

At occupational exposure levels 1,2-dibromo-3-chloropropane has caused serious effects on spermatogenesis without any other signs of intoxication. DBCP should therefore be considered a substance specifically toxic to the testes of man and animals. Animal data show that DBCP also should be considered as a mutagen and a carcinogen.

*Table summarizing the reproductive effects of DBCP*

| Species | Dosage | Effects |
|---|---|---|
| Man | Occup.down to appr. 1 ppm | Decreased sperm count, azoospermia |
| Man | Occup. 8-53 ppb | No effects seen |
| Rat | 12 ppm 7 h/5days/week 70-92 days | 45% mortality |
| Several | 2 ppm 7 h/5 days/week 70-92 days | Testicular atrophy |
| Male rat | 10 ppm 6 h/5 days/week 14 weeks | Testicular atrophy, decreased fertility |
| Female rat | 10 ppm 6 h/5 days/week 14 weeks | No effects seen |
| Male rat | 1 ppm 6 h/5 days/week 14 weeks | No effects seen |
| Male rabbit | 10 ppm 6 h/5 days/week 8 weeks | Mortality, sperm count depression, testicular atrophy |
| Male rabbit | 1 ppm 6 h/5 days/week 14 weeks | Sperm count depression, testicular atrophy |
| Male rabbit | 0.1 ppm 6 h/5 days/week 14 weeks | No effects seen |

*Source:* 'KEMI Report No. 7/92. (Effects on Reproduction of Chloroform and DBCP)'. Nordic Council of Ministers, The Swedish National Chemicals Inspectorate, P.O. Box 1384, S-171 27 Solna, Sweden, (1992).

## *Diethylhexyl phthalate*

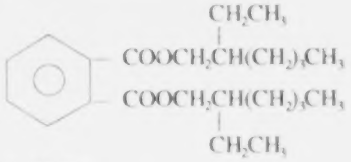
The International Programme on Chemical Safety has published an Environmental Health Criteria document on diethylhexyl phthalate. An International Task Group discussed and finalized the document at the British Industrial Biological Research Association (BIBRA), Carshalton, Surrey, United Kingdom. A summary of the findings of the Task Group which discussed the document is given below.

*Properties and analytical methods*

Di(2-ethylhexyl)phthalate (DEHP) is a benzenedicarboxylic acid ester which at room temperature is a colourless to yellow oily liquid. Its solubility in water is low (0.3-0.4 mg/litre), and is even lower in salt water. It is miscible with most common organic solvents. The volatility of DEHP is relatively low ($8.6 \times 10^{-4}$ Pa).

Many sampling and analytical methods have been developed for the determination of DEHP in different media. Sensitive methods, such as gas chromatography, high-performance liquid chromatography, and mass spectrometry are being used increasingly. Analysis of low concentrations of DEHP is complicated by contamination from plastic equipment during sampling and analysis.

**Identity**

| | |
|---|---|
| *Common name:* | Di(2-ethylhexyl)phthalate |
| *Chemical names:* | |
| IUPAC | phthalic acid bis(2-ethylhexyl) ester |
| CAS | 1,2-benzenedicarboxylic acid bis(2-ethylhexyl) ester |
| *Synonyms:* | DEHP; 1,2-benzenedicarboxylic acid bis(ethylhexyl) ester; bis(2-ethylhexyl) 1,2-benzenedicarboxylate; bis(2-ethylhexyl) ester of phthalic acid; bis(2-ethylhexyl)phthalate; di(2-ethylhexyl) *ortho*-phthalate; di(ethylhexyl) phthalate; dioctyl phthalate; DOP; ethylhexyl phthalate; 2-ethylhexyl phthalate; octyl phthalate; di-*sec*-octyl phthalate; phthalic acid dioctyl ester |
| *Trade names:* | Bisoflex 81; Bisoflex DOP; Compound 889; DAF 68; Ergoplast FDO; Eviplast 80; Eviplast 81; Fleximel; Flexol DOP; Goodrite GP 264; Hatcol DOP; Kodaflex DOP; Mollan O; Nuoplaz DOP; Octoil; Palatinol AH; Platinol DOP; Pittsburgh; PX-138; Reomol DOP; Reomol D 79P; Sicol 150; Staflex DOP; Truflex DOP; Vestinol AH; Vinicizer 80; Witcizer 312 |
| *Chemical structure:* |  |
| *Molecular formula:* | $C_{24}H_{38}O_4$ |
| *Registry numbers:* | |
| CAS | 117-81-7 |
| RTECS | TI 035 000 |

*Physical and chemical properties*

| | |
|---|---|
| *Physical state:* | oily liquid |
| *Colour:* | colourless to yellow |
| *Melting point:* | −46°C |
| *Boiling point:* | 370°C (at atmospheric pressure) |
| *Flash point:* | 425°C (open cup) |
| *Density:* | 0.98 g/ml at 20°C |
| *Vapour pressure:* | $8.6 \times 10^{-4}$ Pa |
| *n-Octanol/water partition coefficient:* | log $P_{ow}$ 3-5 |
| *Solubility in water:* | low (45 µg/litre at 20°C) |
| *Solubility in solvents:* | miscible with most organic solvents |
| *Conversion factors:* | 1 ppm = 15.87 mg/m³<br>1 mg/m³ = 0.063 ppm |

*Uses and sources of exposure*

Almost all the DEHP present in the environment arises from anthropogenic sources rather than from natural ones. The worldwide production of DEHP has been increasing during recent decades and at present amounts to about $1 \times 10^6$ tonnes per year. One-third of the total production is in the USA and one-third in Europe.

DEHP is the most widely used plasticizer (comprising 50% of all phthalate ester plasticizers) that softens resins. It may account for 40% (w/w) or more of the plastic. DEHP is used for making the polyvinyl chloride (PVC) utilized in building, construction and packaging, and for medical device components. Smaller amounts are used in industrial paints and as a dielectric fluid in condensers.

Discarded plasticized products may be disposed of either by incineration or via dumping in a landfill site. During incineration at a low temperature, a large percentage of the DEHP may be lost to the atmosphere. The environmental fate of DEHP in landfill sites has not been well studied and no definite conclusions can be reached.

*Environmental transport, distribution, and transformation*

Transport in the air is the major route by which phthalates enter the environment. From the atmosphere DEHP either falls or is washed out via rainfall. It has a high octanol-water partition coefficient, so the equilibrium between water and an organic-rich soil or sediment is in favour of the soil or sediment. It is readily adsorbed by organic soil particles. Although the solubility of DEHP in water is low, the amount present in surface water may be higher due to adsorption onto organic particles and interaction with dissolved organic matter. It is adsorbed particularly by small particles, and adsorption is enhanced in salt water.

Atmospheric photodegradation of DEHP is rapid, but its chemical hydrolysis in the environment is practically non-existent. Aerobic degradation has been found to be carried out by several soil microorganisms. However, the microbial degradation of DEHP in the environment has been reported to be slow. The biodegradation pathway begins with hydrolysis to the mono-ester, which is then converted to phthalic acid. The ring-opening degradation to pyruvate and succinate and then to $CO_2$ and $H_2O$ is similar to the metabolic pathway of benzoic acid. The aerobic degradation is temperature dependent. Below 10 °C little degradation takes place. At higher temperatures biodegradation proceeds in the upper layer of the soil, but it is virtually non-existent deeper down where conditions are anaerobic. Anaerobic degradation, if it exists, is very much slower than aerobic degradation.

DEHP is highly lipophilic and moderately persistent. The degree of bioaccumulation depends on the capability of an organism to metabolize it. It has been shown to accumulate to a high degree in a variety of aquatic invertebrates, fish, and amphibians.

When DEHP was applied to plant leaves, there was little loss over a 15-day period. Uptake by plants from soil or sewage sludge was found to be low.

*Environmental levels and human exposure*

DEHP exists widely in the environment and is found in most samples, including air, precipitation, water, sediment, soil, and biota. Levels are generally highest in industrialized areas. Concentrations of up to 300 ng/m³ have been found in urban and polluted air. Levels of between 0.5 and 5 ng/m³ have been reported in the air of oceanic areas, and the rainfall in these areas contained up to about 200 ng/litre. Precipitation samples from an area close to a plasticizer production plant indicated that the rate of dry deposition was 0.7 to 4.7 $\mu g/m^2$ per day.

In rivers and lakes the concentration of DEHP has been found to be up to 4 $\mu$g/litre, highest levels being associated with industrial effluent discharge points. The concentration in the sea is less than 1 $\mu$g/litre, highest levels being in estuaries.

Due to its hydrophobic character, DEHP is readily absorbed to soil, sediment, and particulate matter. River sediment levels of up to 70 mg/kg (dry weight) have been reported, and these have reached 1480 mg/kg (dry weight) near discharge points.

The concentration of DEHP in biota varies from less than 1 to 7000 $\mu$g/kg. It has been found in various types of food, such as fish, shellfish, eggs, and cheese. The estimated average exposure was around 300 $\mu$g/person per day in the USA in 1974 and 20 $\mu$g/person per day in the UK in 1986.

Blood transfusions and other medical treatment using plastic devices may lead to involuntary human exposure to DEHP. Levels from 13.4 to 91.5 mg/kg (dry weight) in lung tissue have been detected in patients.

The few data available indicate that workplace concentrations of DEHP are usually below 1 mg/m³.

*Kinetics and metabolism*

Available data on oral administration indicate that DEHP is hydrolysed in the gut by pancreatic lipase. The metabolites formed, i.e. mono(2-ethylhexyl)phthalate (MEHP) and 2-ethylhexanol, are rapidly absorbed. When $^{14}$C-labelled DEHP (2.9 mg/kg) was given orally to rats, more than 50% was recovered in the urine or bile. The bioavailability of an oral dose of DEHP seems to be higher in young rats than in older ones.

When administered orally, DEHP is extensively hydrolysed in the gut in certain animals, e.g., rats, and is mainly distributed as monoethylhexyl phthalate (MEHP). However, hydrolysis occurs to a much lesser extent in primates and humans. MEHP binds to plasma proteins. The liver seems to be the major organ for the metabolism of MEHP and 2-ethylhexanol. Several further metabolites have been identified, $\omega$- and $\omega$-1 -oxidation being the major metabolic pathways. One or several of the products of $\omega$-oxidation may be further metabolized by $\beta$-oxidation. Non-linear kinetics have been observed for the $\omega$-oxidation. DEHP metabolism shows considerable species differences; e.g., the $\omega$-oxidation pathway is less extensive in humans than in rats.

Almost 100% of an oral dose of DEHP (2.9 mg/kg) was recovered in rat faeces and urine after a week. Bile and urine are the major excretory pathways. In a human study, 15-25% of an oral dose (0.45 mg/kg) of DEHP was excreted as MEHP, and oxidized metabolites constituted a major portion of the excretion products.

*Effects on laboratory mammals and in vitro test systems*

The oral $LD_{50}$ for DEHP is about 25-34 g/kg, depending on the species, but the value for MEHP is lower. In feeding studies on rats and mice, DEHP dosages greater than 3 g/kg per day caused deaths within 90 days, and a level of 0.4 g/kg per day reduced weight gain within a few

days. In other studies, 6.3-12.5 g/kg diet caused a body weight reduction.

Hepatomegaly and increased relative kidney weights have been observed in treated animals in long-term studies. In one study, there were also hypertrophic cells in the anterior pituitary.

Several studies have shown testicular atrophy, evident within a few days, related to DEHP administration (dietary levels of 10-20 g DEHP/kg). Younger rats seem to be more susceptible than older ones, and rats and mice seem to be more sensitive than marmosets and hamsters. Reversibility of the atrophy has been observed. MEHP has toxic effects on Sertoli cells *in vitro*. DEHP, as well as MEHP, shows teratogenic properties. Malformations were observed at dietary levels of 0.5-2 g/kg in mice, and embryotoxic effects were observed at dietary levels greater than 10 g/kg.

Tests for mutagenicity and related end-points have been negative in most studies. DEHP may induce cellular transformation, and it has been shown to be carcinogenic at doses of 6 and 12 g DEHP/kg diet in rats and 3 and 6 g/kg diet in mice. There was a dose-related increase in hepatocellular tumours in both sexes of both species. The induction of hepatic peroxisome proliferation and cell replication is strongly associated with the liver carcinogenic effect of certain non-genotoxic carcinogens including DEHP. However, marked differences have been observed among animal species with respect to DEHP-induced peroxisome proliferation.

In contrast to rat hepatocytes, DEHP metabolites do not produce peroxisome proliferation in cultured human hepatocytes.

*Effects on humans*

Only very limited information is available on the effects of DEHP on humans. Mild gastric disturbances, but no other deleterious effects, were reported for two subjects given 5 or 10 g DEHP.

*Effects on other organisms in the laboratory and field*

Most studies have yielded nominal $LC_{50}$ values in acute toxicity tests that are in excess of 10 mg/litre, values which give a low toxicity rating for DEHP. However, these levels exceed the DEHP water solubility (0.3-0.4 mg/litre). One study suggested greater sensitivity of the water flea *Daphnia pulex*, with a nominal 48-h $LC_{50}$ of 0.133 mg/litre. The only acute test with measured DEHP concentrations was on the fathead minnow and revealed a 96-h $LC_{50}$ of >0.33 mg/litre. In prolonged studies, the no-observed-effect level (NOEL) for *Daphnia magna* was 72 µg/litre. For adult fish a NOEL of > 62 µg/litre was determined. An exposure of 14 µg/litre, from 12 days prior to hatching, caused a significant increase in trout fry mortality. DEHP concentrations of between 3.7 and 11 µg/litre led to a reduction in the vertebral collagen of fish.

The survival of zebra fish fry is adversely affected by DEHP concentrations of 50 mg/kg food. Sediment concentrations of 25 mg/kg (w/w) significantly reduced microbial activity and the number of tadpoles hatching.

The acute toxicity of DEHP to algae, plants, earthworms, and birds is low.

*Evaluation*

DEHP causes reproductive and hepato-carcinogenic effects in rats and mice. Testicular atrophy is the main reproductive effect in rats and mice, and young animals are more susceptible than older ones to this effect. The induction of hepatic peroxisome proliferation and cell replication are strongly associated with the liver carcinogenic effect of certain non-genotoxic carcinogens including DEHP. However, marked differences have been observed among animal species with respect to DEHP-induced peroxisome proliferation. Currently there is not sufficient evidence to suggest that DEHP is a potential human carcinogen.

There is no documented information that DEHP presents any hazard, based on acute exposure to fish and daphnids. However, a reduction of microbial activity in sediment at environmental levels of DEHP was reported. A comparison between environmental levels and the concentrations that produce effects in prolonged studies, especially early life-stage tests on fish and amphibians, indicates that a hazard for the environment, particularly via water and sediment, cannot be excluded. Adverse effects on organisms are likely in areas with highly contaminated water and sediments which are near to point emission sources.

Although few relevant studies have been reported, the acute toxicity of DEHP to algae, plants, earthworms, and birds appears to be low.

*A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case Postale 356, 15 Chemin des Anémones, CH-1219 Châtelaine, Geneva, Switzerland.*

Source: 'Environmental Health Criteria 131: Diethylhexyl phthalate.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1992).

## *Isobenzan*

The International Programme on Chemical Safety has published an Environmental Health Criteria document on isobenzan. An International Task Group discussed and finalized the document in Geneva, Switzerland. In addition IPCS has published a Health and Safety Guide (HSG) on isobenzan. A summary of the findings of the Task Group which discussed the criteria document is given below.

*Evaluation*

As far as is known, isobenzan, an organochlorine insecticide, was only manufactured during the period 1958-65. It was used from existing stocks for several years thereafter. At present, the only major sources of exposure are believed to be the original waste-disposal sites of industrial wastes or dredgings from contaminated sediments.

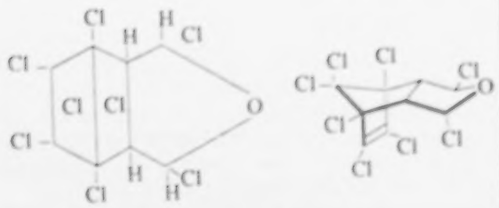
After isobenzan is applied to soil, a rapid initial loss occurs, after which the remaining compound decays at a much slower rate. It persists in soil from 2 to 7 years depending on the type of soil. Under laboratory conditions isobenzan decomposes in surface water within a few weeks when exposed to natural or artificial light.

Soil, groundwater, and surface water from polders built up using sediment contaminated with organochlorine, including chlorinated cyclodiene compounds, still contained minor residues of isobenzan some years later. In 1979-80, no isobenzan was detected (detection limit: 0.01 mg/kg dry

**Identity**

| | |
|---|---|
| *Common name:* | Isobenzan |
| *Chemical name:* | 1,3,4,5,6,7,8,8-octachloro-4,7-methylene-3a,4,7,7a-tetrahydro-isobenzofuran |
| *Synonyms and trade names:* | BAS-4402; CP 14957; ENT-25 545; OMS-206; OMS-618; SD-4402; WL 1650; preparation 948; Telodrin (technical product); Omtan |

*Chemical structure:*



*Molecular formula:* $C_9H_6OCl_8$

*Registry numbers:*

| | |
|---|---|
| CAS | 297-78-9 |
| RTECS | PC 1225 000 |

*Physical and chemical properties*

| | |
|---|---|
| *Physical state:* | crystalline powder |
| *Colour:* | whitish to light brown |
| *Odour:* | mild 'chemical' odour |
| *Relative molecular mass:* | 411.73 |
| *Melting point (°C):* | 120-122 |
| *Flash point:* | non-flammable |
| *Explosion limits:* | non-explosive |
| *Relative density:* | 1.87 |
| *Vapour pressure (20°C):* | $6.7 \times 10^{-4}$ Pa ($5 \times 10^{-6}$ mmHg) |
| *Solubility in water:* | practically insoluble |
| *Solubility in organic solvents:* | slightly soluble in kerosene and ethanol; soluble in acetone, benzene, toluene, xylene, heavy aromatic naphtha, and ethyl ether |
| *Stability:* | relatively stable to acids; dehydrochlorination may occur under strong alkaline conditions |

weight) in the sediment of rivers in The Netherlands. Following soil treatment, residues in crops are usually low (below 0.05 mg/kg crop), but higher levels may be found in some root crops (up to 0.2 mg/kg in carrots). In market surveys conducted during the time of the agricultural use of isobenzan, no residues were detected in the food items analysed (less than 0.01 mg/kg).

After cattle were allowed to graze pastures treated with isobenzan, the resultant daily products contained residues of the insecticide. Two samples of butter contained 0.07 and 0.15 mg isobenzan/kg product, while the levels in whole milk were 0.005 to 0.07 mg/kg. Dried milk, however, contained only 0.005 mg/kg. During the processing of dairy products, up to 50% of the residue was lost, depending on the type of treatment.

No data are available on the levels of isobenzan in the blood or adipose tissue of the general population. Operators exposed to isobenzan in manufacturing and formulation plants had mean whole blood levels of up to 0.041 mg/litre. In whole blood samples of people living in the neighbourhood of one plant, the concentration of isobenzan was below the limit of detection (0.001 mg/litre). Isobenzan is readily absorbed through the gastrointestinal wall and is transported in the blood as the unchanged compound. Hydrophilic metabolites are formed, one of which has been identified as isobenzan lactone. Isobenzan accumulates in the tissues and organs of rats and dogs in the following order: fat > liver = muscle > brain > blood. The tissue concentrations of female rats are generally higher than those of males, especially in body fat. The biological half-life in body fat was found to be 10.9 days in male rats and 16.6 days in female rats. A female canine pup, whose blood contained 0.09 mg isobenzan/litre, showed convulsions 15 days after birth. The pup had only fed on the milk of its mother, a Beagle hound that had been dosed with isobenzan and whose milk contained 0.7 mg/litre. Similar effects on pups were seen in a rat reproduction study. Isobenzan is excreted via the milk of cows.

Mosquito larvae and soil fungi metabolize isobenzan in the same way as vertebrates, yielding isobenzan lactone as a metabolite.

Isobenzan is very persistent in the environment and bioaccumulates. It is highly toxic to fish, shrimps, and birds. In The Netherlands, the country where isobenzan was manufactured, residues in the eggs of terns living along the Dutch coast ranged up to 0.45 mg/kg (mean, 0.09 mg/kg), while mean residues in mussels and fish were 0.05 mg/kg in 1965. Earthworm numbers were found to be reduced in field plots treated with isobenzan at 2 kg/ha. Nitrification was reduced, with a consequent increase in inorganic nitrogen, in soils treated with isobenzan in the field at 1 kg/ha, although laboratory studies showed no effect on nitrification at doses equivalent to 250 g/ha.

The acute toxicity of isobenzan to mammals is high, both by the oral and percutaneous routes. The mode of action of its toxicity is an overstimulation of the central nervous system, resulting in convulsions. The acute toxicity of formulations of isobenzan reflects the percentage of active ingredient present.

Isobenzan is not a skin irritant, but some formulated products may cause irritation.

Limited short- and long-term oral studies in mice, rats, and dogs have shown that isobenzan may cause histological changes of the classical type of organochlorine intoxication in the liver. In a long-term rat study, a no-observed-effect level of 5 mg/kg diet (approximately 0.25/kg body weight) was determined, and in a 2-year dog study the no-observed-adverse-effect level (NOAEL) was 0.025 mg/kg body weight.

A one-generation reproduction study in rats indicated a NOAEL of 0.1 mg/kg diet (approximately 0.005 mg/kg body weight). At a level of 1 mg/kg diet (approximately 0.05 mg/kg body weight) the survival of pups decreased.

No teratogenicity or mutagenicity studies have been reported. No carcinogenic potential was demonstrated in a 2-year oral study on rats and in an oral study on mice, but these studies were inadequate to evaluate carcinogenicity.

The toxicological data base for isobenzan is incomplete. In general, the quality of the data is considered to be poor by today's standards and inadequate for an evaluation of the hazards to human health or the environment.

Data on exposed humans are limited to studies on workers in a factory in the Netherlands during the manufacture and formulation of isobenzan and related 'chlorinated cyclodiene insecticides'. No cases of skin irritation were reported. In several cases of intoxication, convulsions occurred but the changes in the EEG pattern were reversible. The intoxication threshold level (for convulsions) was estimated to be 0.015 mg isobenzan/litre blood, and the biological half-life of isobenzan in human blood was estimated to be of the order of 2.8 years.

*Conclusions and recommendations*

Isobenzan is highly toxic and very persistent. The available information on the hazards of isobenzan is incomplete, but is, nevertheless, sufficient to indicate that the hazard it poses to those who handle it and to the environment is such that no human or environmental exposure to this substance, used either as an insecticide or for any other purpose, should be allowed.

*A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case Postale 356, 15 Chemin des Anémones, CH-1219 Châtelaine, Geneva, Switzerland.*

Sources: 1. 'Environmental Health Criteria 129: Isobenzan.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1992).

2. 'Health and Safety Guide No 61: Isobenzan.' International Programme on Chemical Safety (1992).

## *Trichlorfon*

The International Programme on Chemical Safety has published an Environmental Health Criteria document on trichlorfon. An International Task Group discussed and finalized the document in Geneva, Switzerland. In addition IPCS has published a Health and Safety Guide (HSG) on trichlorfon. A summary of the findings of the Task Group which discussed the criteria document is given below.

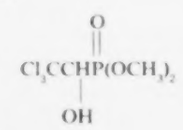
Trichlorfon is a colourless crystalline powder stable at room temperature. It is slowly hydrolysed in acid media; the half-life is 526 days at pH 1-5 and 20°C. Cleavage of one of the methyl ester groups takes place by acid hydrolysis. In alkaline media, however, trichlorfon is rapidly converted to dichlorvos and then to hydrolytic products.

*Exposure*

Trichlorfon is an organophosphorus insecticide that has been in use since the early 1950s. In agriculture, it is mainly used against insect pests in field and fruit crops. Trichlorfon is also used to control forest insects and for the control of parasites in domestic animals. Under the name of metrifonate, trichlorfon is used for the treatment of human infestation by *Schistosoma haematobium*. It is considered to be a slow release reservoir of dichlorvos. Trichlorfon is available in the form of an emulsifiable concentrate, powder, dust, granules, solution, and ultra-low volume concentrates.

The air concentration of trichlorfon insecticide may be as high as 0.1 mg/m³, soon after spraying, but levels decrease within days to below 0.01 mg/m³. Levels of tri-

**Identity**

| | |
|---|---|
| *Common name:* | Trichlorfon (ISO) |
| *Chemical name:* | Dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate |
| *Synonyms:* | chlorofos; DEP; DETF; dipterex; dimethyl 1-hydroxy-2,2,2-trichloro-ethanephosphonate; *O,O*-dimethyl (2,2,2-trichloro-1-hydroxyethyl) phosphonate; metrifonate; foschlor; trichlorofon; trichlorphon |
| *Trade names:* | Agroforotox; Anthon; L 13/59; Bilarcil; Cekufon; Danex; Dipterex; Ditriphon; Dylox; Dyrex; Dyvon; Masoten; Metrifonate; Neguvon; Proxol; Tugon; Wotex |
| *Chemical structure:* |  |
| *Molecular formula:* | $C_4H_8Cl_3O_4P$ |
| *Registry numbers:* | |
| CAS | 52-68-6 |
| RTECS | TA 0700000 |

*Physical and chemical properties*

| | |
|---|---|
| *Physical state:* | colourless crystals |
| *Melting point (°C):* | 83-84 |
| *Boiling point (°C)* | 100 (0.1 mmHg) |
| *Vapour pressure (20°C):* | $7.8 \times 10^{-6}$ mmHg |
| *Volatility (20°C):* | 0.022 mg/m³ |
| *Density:* | 1.73 (20°/4°C) |
| *Solubility in g/100 ml (25°C):* | water 15.4<br>benzene 15.2<br>chloroform 75.0<br>diethyl ether 17.0<br>*n*-hexane 0.08 |
| *Octanol/water partition coefficient:* | log $P_{ow}$ 0.57 |
| *Corrosiveness:* | corrosive to metals |
| *Conversion factors:* | *1 ppm = 11.4 mg/m³*<br>*1 mg/m³ = 0.088 ppm, at 25°C and 760 mmHg* |

chlorfon in run-off water from sprayed areas may be as high as 50 μg/litre, though levels in surface waters are usually much lower and decrease rapidly.

Trichlorfon degrades rapidly in soil, and levels generally decrease to negligible amounts within one month of application. It is relatively stable in water below pH 5.5. At higher pH, trichlorfon is transformed to dichlorvos. While microorganisms and plants may metabolize trichlorfon, the most important route of removal is abiotic hydrolysis.

With a few exceptions, levels of trichlorfon on crops are below 10 mg/kg the day after application, and fall to below 0.1 mg/kg during the two weeks following.

Milk from cows treated with trichlorfon for pest control may contain residues as high as 1.2 mg/litre 2 h after application, but the levels decline to below 0.1 mg/litre 24 h after treatment. Significant levels of trichlorfon have not been found in meat from treated animals. Eggs from treated hens have been found to contain 0.05 mg trichlorfon/kg.

*Uptake, metabolism, and excretion*

Trichlorfon is readily absorbed via all routes of exposure (oral, dermal, inhalation) and is rapidly distributed to the tissues of the body. Peak blood concentrations were detected within 1-2 h, almost total disappearance from the blood stream occurring in a matter of 1.5-4 h. The biological half-life of trichlorfon in the mammalian blood was estimated to be in the range of 30 min.

Trichlorfon undergoes transformation to dichlorvos (2,2-dichlorovinyl dimethyl phosphate), via dehydrochlorination, in water, biological fluids, and tissues, at pH values higher than 5.5. Dichlorvos is the physiologically active anticholinesterase. The main routes of degradation are demethylation, P-C bond cleavage, and ester hydrolysis via dichlorvos. The major metabolites of trichlorfon found *in vivo* are demethyl trichlorfon, demethyl dichlorvos, dimethyl hydrogen phosphate, methyl hydrogen phosphate, phosphoric acid, and trichloroethanol. The last metabolite is found in the urine as a glucuronide conjugate.

Trichlorfon and metabolic products are primarily eliminated via the urine. Studies conducted with radiolabelled ($^{14}$C-methyl and $^{32}$P-) trichlorfon revealed that the bulk of the chemical was eliminated in the form of water-soluble material, little being chloroform-soluble. Some 66-70% of the water-soluble products appeared in the urine within 12 h while 24% of the $^{14}$C-methyl material was eliminated in the expired air as carbon dioxide ($CO_2$). Low levels of trichlorfon and metabolites have been detected in bovine milk following oral and dermal treatment of the animals.

*Effects on organisms in the environment*

Trichlorfon is moderately toxic for fish (96-h $LC_{50}$ values range between 0.45 mg/litre and 51 mg/litre) and moderately to highly toxic for aquatic arthropods (48-h/96-h $LC_{50}$ values range between 0.75 μg/litre and 7800 μg/litre). However, reported concentrations of trichlorfon in surface waters, after application in forests at 6 kg/ha, fall short of these ranges. Thus, in normal usage, trichlorfon will have little or no effect on populations of aquatic organisms, since other groups, such as molluscs and microorganisms are less sensitive than arthropods. $LD_{50}$ values from laboratory studies ranging from 40 mg/kg to 180 mg/kg indicate that trichlorfon is moderately toxic for birds. However, in field studies, no effects on numbers, breeding pairs, nesting success, or mortality of forest songbirds were seen following aerial application of trichlorfon. An observed reduction in singing and increased feeding activity may have been the result of a reduction in food organisms. There is no indication that trichlorfon will adversely affect organisms in the terrestrial environment, other than arthropods. There is no information on effects beneficial to arthropods.

*Effects on experimental animals and* in vitro *test systems*

Trichlorfon is an insecticide that is moderately toxic for experimental animals. Oral $LD_{50}$ values for technical trichlorfon in laboratory animals range from 400 to 800 mg/kg body weight and dermal $LD_{50}$ values for the rat are greater than 2000 mg/kg body weight.

Trichlorfon poisoning causes the usual organophosphate cholinergic signs attributed to accumulation of acetylcholine at nerve endings.

Technical trichlorfon was shown to be moderately irritating to the eyes of rats, but was not irritating in skin tests on rabbits. Skin sensitization potential was demonstrated in guinea-pigs.

Short-term, oral toxicity studies were carried out on rats, dogs, monkeys, rabbits, and guinea-pigs. In a 16-week study on rats, a 4-year study on dogs, and a 26-week study on monkeys, no-observed-effect levels (NOELs) of 100 mg/kg diet, 50 mg/kg diet, and 0.2 mg/kg body weight (based on plasma, erythrocyte, or brain ChE activity) respectively, were determined. Inhalation exposure of rats, over 3 weeks, indicated a NOEL of 12.7 mg/m$^3$, based on the inhibition of plasma, erythrocyte, and brain ChE activity. Long-term toxicity/carcinogenicity studies were carried out on mice, rats, monkeys, and hamsters after oral, intraperitoneal, or dermal administration. An adverse effect on the gonads was seen following the oral exposure of mice and rats at dose levels of 30 mg/kg body weight and 400 mg/kg diet, respectively. In a 24-month study on rats and a 10-year study on monkeys, no-observed-adverse-effect levels (NOAELs) of 50 mg/kg diet and 0.2 mg/kg body weight, respectively, were determined. Available data do not provide evidence of carcinogenicity following the long-term exposure of test animals by several routes of administration.

Under physiological conditions, trichlorfon has been reported to have a DNA-alkylating property. The trichlorfon mutagenicity results have been both positive and negative. Dichlorvos may be responsible, either in part or in full, for the effects observed. Most of the *in vitro* mutagenicity studies on both bacterial and mammalian cells were positive while few of the *in vivo* studies produced a positive result.

Studies on mice, rats, and hamsters indicate that trichlorfon produces a teratogenic response in rats at doses high enough to produce maternal toxicity. Exposure of rats to 145 mg trichlorfon/kg diet, during gestation, caused foetal malformations. A gavage dose of 400 mg/kg body weight in hamsters also produced both maternal toxicity and a teratogenic response. The lowest dose by gavage that produced teratogenic effects in rats was 80 mg/kg body weight. The effects appear to be time specific in the gestation period. A NOEL of 8 mg/kg was determined in this gavage study.

NOELs of 8 mg/kg body weight and 200 mg/kg body weight were demonstrated for rats and hamsters, respectively. Teratogenic responses involving the central nervous system have also been reported for the pig and guinea-pig. However, no teratogenic effects were observed in a

3-generation reproduction study on rats, in which high dose levels induced adverse reproductive effects. The NOEL in this study was 300 mg/kg diet.

Very high doses have produced neurotoxic effects in animals. The active transformation product in mammals is dichlorvos, which is estimated to be at least 100 times more potent as an anticholinesterase than trichlorfon.

*Effects on human beings*

Several cases of acute poisoning from intentional (suicide) or accidental exposure have occurred. Signs and symptoms of intoxication were characteristic of AChE inhibition, such as exhaustion, weakness, confusion, excessive sweating and salivation, abdominal pains, vomiting, pinpoint pupils, and muscle spasms. In severe cases of poisoning, unconsciousness and convulsions developed and death usually resulted from respiratory failure. In cases where victims survived due to medical intervention, a delayed polyneuropathy, associated with weakness of the lower limbs, sometimes occurred a few weeks after exposure. In fatal cases, autopsy findings showed ischaemic changes in the brain, spinal cord, and vegetative ganglia, damage to the myelin sheath in the spinal cord and brain peduncles, and structural changes in the axons of peripheral nerves.

A few cases of occupational poisoning have occurred, mainly through the neglect of safety precautions. Occupational exposure at a work-place where air concentrations exceeded 0.5 mg/m$^3$ resulted in decreased plasma cholinesterase and changes in the EEG pattern. However, these were completely reversible on cessation of exposure. No case of skin sensitization have been reported.

This compound has been extensively used for the treatment of schistosomiasis in humans. Administration of a single dose (7-12 mg/kg) resulted in cholinesterase inhibition in plasma and erythrocytes in the range of 40-60%, without cholinergic symptoms. However, mild symptoms were observed in cases with a repeated dose regimen. A high dose level (24 mg/kg) caused severe cholinergic symptoms.

*Conclusions*

—Trichlorfon is a moderately toxic organophosphorus ester insecticide. Over-exposure from handling during manufacture or use and accidental or intentional ingestion may cause serious poisoning.
—Trichlorfon exposure of the general population occurs mainly as a result of agricultural and veterinary practices, and in the treatment of *Schistosoma haematobium*.
—The reported trichlorfon intakes are far below the Acceptable Daily Intake established by FAO/WHO and should not constitute a health hazard for the general population.
—With good work practices, hygienic measures, and safety precautions, trichlorfon is unlikely to present a hazard for those occupationally exposed.
—Despite its high toxicity for non-target arthropods, trichlorfon has been used with few or no adverse effects on populations of organisms in the environment.

*Recommendations*

—For the health and welfare of workers and the general population, the handling and application of trichlorfon should only be entrusted to competently supervised and well-trained operators, who will follow adequate safety measures and apply trichlorfon according to good application practices.
—The manufacture, formulation, agricultural use, and disposal of trichlorfon should be carefully managed to minimize contamination of the environment, particularly surface waters.
—Regularly exposed worker and patient populations should undergo periodic health evaluations.
—Application rates of trichlorfon should be limited, to avoid effects on non-target arthropods. The insecticide should never be sprayed over water bodies or streams.

*A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case Postale 356, 15 Chemin des Anémones, Ch-1219 Châtelaine, Geneva, Switzerland.*

*Sources:* 1. 'Environmental Health Criteria 132: Trichlorfon.' International Programme on Chemical Safety, World Health Organization, CH-1211 Geneva 27, Switzerland (1992).
2. 'Health and Safety Guide No 66: Trichlorfon.' International Programme on Chemical Safety (1992).

## *Xylenes*

The Health and Safety Executive of the United Kingdom has published a Toxicity Review on xylenes. Below is the summary of the findings including an evaluation by IARC. Some information on identifiers, synonyms, properties, production and use of xylenes taken from other sources has been added for the convenience of the reader.

*Production and use*

*Production.* Xylene occurs in petroleum stock, but in very small quantities. It is produced primarily by the catalytic reforming of naphtha streams, which are rich in alicyclic hydrocarbons. The aromatic reformate fractions consist mainly of benzene, toluene and mixed xylenes, xylenes representing the largest fraction. The xylene isomers are separated from the reformate by extraction and distillation on the basis of differences in boiling point. *ortho*-Xylene, which has the highest boiling point, is separated as the bottom distillate; *para*-xylene is separated by continuous crystallization or adsorption from the mixed xylenes or isomerized from the *meta*-xylene/*para*-xylene distillate; and *meta*-xylene is obtained by selective crystallization or solvent extraction of *meta-para* mixtures.

Another source of mixed xylenes is pyrolysis gasoline, a by-product that results from cracking of hydrocarbon feeds during olefin manufacture. The mixed xylene content of pyrolysis gasoline varies, depending upon the feed and the severity of the cracking process. Pyrolysis gasoline is a less efficient source for recovery of mixed xylene than catalytic reformate because it contains large amounts of ethylbenzene.

Mixed xylenes may also be produced from petroleum refining operations by the Toyo Rayon and Atlantic-Richfield processes, in which toluene is transalkylated or disproportionated. Xylenes are marketed principally as mixture of *ortho*, *meta* and *para* isomers, generally referred to as mixed isomers. The individual isomers are also available commercially.

**Identity**

*Common name:* Xylenes

*Chemical names:*

IUPAC: Xylene (*ortho*-, *meta*-, *para*-)

CAS: 1,2-Dimethylbenzene
1,3-Dimethylbenzene
1,4-Dimethylbenzene

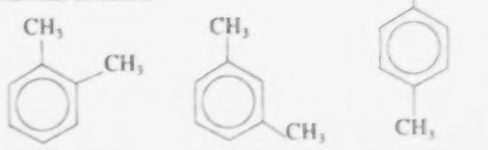
*Synonyms:*

*ortho*-xylene:
*ortho*-dimethylbenzene;
*ortho*-methyltoluene;
2-methyltoluene; 1,2-xylene;
*ortho*-xylol.

*meta*-xylene: *meta*-dimethylbenzene;
*meta*-methyltoluene;
3-methyltoluene; 1,3-xylene;
*meta*-xylol.

*para*-xylene: *para*-dimethylbenzene,
*para*-methyltoluene;
4-methyltoluene; 1,4-xylene;
*para*-xylol

*Chemical structure:*



*ortho*-xylene (1,2-dimethylbenzene) | *meta*-xylene 1,3-dimethylbenzene | *para*-xylene 1,4-dimethylbenzene

*Molecular formula:* $C_8H_{10}$

*Registry numbers:*

CAS: 95-47-6 (*ortho*-xylene)
108-38-3 (*meta*-xylene)
106-42-3 (*para*-xylene)

RTECS: ZE 2450 000 (ortho-xylene)
ZE 2275 000 (meta-xylene)
ZE 2625 000 (para-xylene)

*Use.* Mixed xylenes recovered from all sources (petroleum refineries, pyrolysis gasoline, coal-tar) are used in the chemical and solvent industries. Although isolated xylenes are also blended into gasoline to improve octane rating, the reformate without isolation of mixed xylenes or other aromatics is primarily used for gasoline blending. Unleaded premium gasoline has been reported to contain 10-22% xylenes. Mixed xylenes are also used in the manufacture of perfumes, insecticides, pharmaceuticals and adhesives and in painting, printing, rubber, plastics and leather industries.

In the USA, most of the production of isolated mixed xylenes is separated into the individual isomers for use as chemical intermediates or as solvents. The approximate distributions of the production of mixed xylenes in the USA are as follows: *para*-xylene, 50-60%; gasoline blending, 10-25%; *ortho*-xylene, 10-15%; solvents, 10%; ethylbenzene, 3%; and *meta*-xylene, 1%. *para*-Xylene is used principally to manufacture terephthalic acid and dimethylterephthalate, used in the production of saturated polyester resins and fibres. *ortho*-Xylene is used primarily as a feedstock for the manufacture of phthalic anhydride. It is also used as a chemical intermediate in synthesis of dyes, pharmaceuticals and insecticides. *meta*-Xylene is used in the manufacture of isophthalic acid for polyester resins, and as a chemical intermediate for dyes and insecticides.

*Metabolism*

Vapours of xylenes are rapidly absorbed via the respiratory tract. Xylenes are well-absorbed orally in animals and liquid *meta*-xylene has been shown to be well-absorbed through human skin. Xylenes are highly soluble in blood and fat, and are widely distributed in the body. Only a small proportion of absorbed *meta*-xylene has been detected in human subcutaneous fat. Although accumulation of xylenes in human blood and in animal body fat and brain tissue has been demonstrated during exposure for 1 to 2 weeks, concentrations in animal fat fell on prolonged

*Chemical and physical properties*

| Property | *ortho*-xylene | *meta*-xylene | *para*-xylene |
|---|---|---|---|
| *Description:* | | Clear, colourless liquid | Crystalline solid |
| *Boiling point (°C)* | 144.4 | 139.1 | 138.3 |
| *(at 10 mmHg):* | 32 | 28.1 | 27.2 |
| *Melting point (°C):* | −25.2 | −47.9 | 13.3 |
| *Density (20°/4°C):* | 0.8802 | 0.8642 | 0.8611 |
| *Refractive index (20°C):* | 1.5055 | 1.4972 | 1.4958 |
| *Spectroscopy data:* | Infrared, ultraviolet and nuclear magnetic resonance spectral data have been reported | | |
| *Solubility:* | Soluble in ethanol, diethyl ether, acetone, benzene; insoluble in water | | |
| *Volatility (vapour pressure, mm) (25°C):* | 6.8 | 8.3 | 8.9 |
| *Flash point (°C):* | 32 | 29 | 27 |
| *Octanol/water partition coefficient (log P):* | 2.77-3.12 | 3.2 | 3.15 |
| *Conversion factor:* | $mg/m^3 = 4.34 \times ppm$ | | |
| *Reactivity:* | Highly inflammable | | |

exposure (possibly due to xylenes inducing their own metabolism). Low levels of xylenes and their metabolites have been detected in the foetuses of exposed rodents. Xylenes are extensively metabolized in humans, with about 90% of the absorbed dose being excreted in urine as the glycine conjugate of methylbenzoic acid following inhalation of up to 200 ppm vapour or dermal exposure to the liquid. There is evidence that excretion of methylbenzoic acid conjugates can be reduced by exposure to certain other chemicals. No significant differences in the disposition and metabolism of the three xylene isomers have been demonstrated in humans, although some quantitative differences have been identified in animals.

*Toxicity to animals*

Xylenes have a low acute toxicity. Inhalation $LC_{50}$ values in excess of 4000 ppm and oral $LD_{50}$ values in excess of 3500 mg/kg have been reported. Death is caused by respiratory failure due to CNS depression. At high vapour concentrations there is a major effect on the CNS and a biphasic response with initial excitation followed by depression, particularly for *para*-xylene, has been observed. Elevated serum hepatic enzyme levels and decreased lung cytochrome P450 levels have been noted. Vapours of xylenes are respiratory tract irritants.

Single application of liquid xylenes can cause overt skin irritation. Eschar formation and blistering have been reported after repeated exposure. A single instillation of liquid xylenes into the eye caused predominantly slight conjunctival irritation. No skin sensitization data are available.

Hearing loss, mainly at high frequencies, was the major finding with sub-acute exposure. It was observed following repeated exposure to 800 ppm and above for 6 weeks or to 1450 ppm for 3 days. A no-effect level was not determined and reversibility was not assessed. Apart from this single study of hearing loss, xylenes have been shown to have low toxicity following repeated inhalation exposure and oral administration. The most commonly reported finding was a functional hypertrophy of the liver observed at exposure levels of 50 ppm and above.

There is no evidence from numerous studies with different end-points that xylenes are genotoxic. There is no evidence of carcinogenicity due to xylenes, following chronic oral administration, in the rat or mouse; the data for the male rat are, however, limited.

In reproductive toxicology studies there is no evidence of teratogenicity following inhalation exposure but delayed development has been observed. Following oral administration teratogenicity was observed at 683 mg/kg (*ortho*- and *para*-xylene) and 870 mg/kg (*meta*-xylene). These dose levels were at or above those causing increased resorptions.

*Toxicity to humans*

Following single inhalation exposure or oral ingestion, the signs of toxicity predominantly involve the CNS. Headache, nausea and vomiting, dizziness and vertigo have all been reported at an inhalation exposure level estimated to be 700 ppm. In controlled exposure studies, a slight impairment of vestibular and visual functions and reaction time was observed at exposure levels of 200 ppm *meta*-xylene and above; no effects were noted at exposure levels of up to 160 ppm. Death, attributed to respiratory depression following loss of consciousness, has been observed, with an exposure level required for loss of consciousness being estimated as 10,000 ppm. Apparent complete recovery was observed in survivors. There was evidence of an interaction between *meta*-xylene and ethanol (resulting in further impairment of visual functions and reaction times) at low *meta*-xylene levels (145-150 ppm) with a functional tolerance developing at higher exposure levels (275-290 ppm).

Exposure to vapours of xylenes at concentrations of 200 ppm and above has caused eye, nose and throat irritation. Corneal lesions have been documented following occupational exposure to xylene vapour. Liquid xylenes are irritant to human skin and eyes. Xylenes did not result in sensitization in a skin sensitization study and there is no evidence, despite widespread use, that xylenes cause sensitization by skin contact.

In controlled, repeated-exposure studies there was no evidence of accumulative effects but there was some evidence of tolerance or adaptation. Following repeated exposure of workers to xylenes, or solvents containing significant amounts of xylenes, episodes of depression, extreme fatigue, anxiety and sleep disorders were frequently reported. There was a gradual reduction in the severity of most symptoms after cessation of exposure. Insufficient data are available for any conclusions to be made on the effects of xylenes on neurophysiological or psychological functions, liver or kidney function or haematology parameters. Much of the data comes from studies on occupational groups such as painters and printers who have a mixed pattern of solvent exposure.

Similarly, insufficient data are available for any conclusions to be made on the genotoxic or carcinogenic potential of xylenes or on the potential effects on reproduction.

*An evaluation by IARC*

The International Agency for Research on Cancer Working Group on the Evaluation of Carcinogenic Risks to Humans made the following evaluation on xylene.

There is *inadequate evidence* for the carcinogenicity of xylene in humans. There is *inadequate evidence* for the carcinogenicity of xylene in experimental animals. The overall evaluation was that xylene is *not classifiable as to its carcinogenicity to humans* (Group 3).

*Sources:* 1. 'Toxicity Review No 26: Xylenes.' United Kingdom, Health and Safety Executive, H.M. Stationery Office, 49 High Holborn, London WCIV 6HB, UK (1992).

2. *IARC Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans: Some organic solvents.* Vol. 47, IARC, Lyon, France (1989).

# IV. General legislation on chemicals

## European Economic Community

### Export and Import of Certain Dangerous Chemicals

The Council of the European Communities on 29 August 1992 published, in its *Official Journal*, Council Regulation (EEC) No. 2455/92 of 23 July 1992 concerning the export and import of certain dangerous chemicals. The following is a summary of the background and the Articles of this Regulation.

*Background*

Hitherto, certain provisions of Community legislation, and in particular Directive 19/117/EEC (Bulletin Vol. 10 No. 2) restricted the marketing and use of certain dangerous substances and preparations and prohibited the placing on the market and use of plant protection products containing certain active substances in the Member States; however these provisions do not apply to such products when intended for export to third countries.

Directive 67/548/EEC[1] specifies the requirements for packaging and labelling of dangerous chemicals when they are intended for export to third countries and ensures that the rules applicable within the Community should apply to such chemicals.

The international trade in certain chemicals which are banned or severely restricted in countries of export has caused international concern on the grounds of the protection of man and the environment. Measures are necessary for such protection in both the Community and all other countries.

Schemes for notification, information and Prior Informed Consent (PIC) concerning international trade in such substances have been set up within the framework of international organizations, namely the Organization for Economic Cooperation and Development, UNEP and the FAO. The Community and its Member States have actively participated in the work of these international organizations relating to banned and severely restricted substances and it was therefore considered appropriate that the Community acts upon the results of this work through uniform Community procedures.

The export of chemicals to which this Regulation applies should be made subject to a common notification procedure which would permit the Community to notify third countries with regard to such exports. It is also necessary to inform all the Member States of notifications received from third countries with regard to imports of substances banned or severely restricted under the legislation of those countries. The common notification procedures should also provide a basis for an appropriate exchange of information within the Community, including information on the implementation of the international notification scheme.

To this end, the Commission will report to the European Parliament and the Council at regular intervals, in particular on any possible reaction from the country of destination. Resolution 88/C 170/2[2] invited the Commission to submit proposals for adapting Regulation No. 1734/88 with a view to introducing a PIC scheme similar to that established by UNEP and FAO. The Articles and Annexes of this new Regulation are as follows.

*Article 1: Objectives*

1. The purpose of this Regulation is to establish a common system of notification and information for imports from and exports to third countries of certain chemicals which are banned or severely restricted on account of their effects on human health and the environment and to apply the international notification and 'prior informed consent' (PIC) procedure established by the United Nations Environment Programme (UNEP) and the Food and Agriculture Organization (FAO[3].)
2. The purpose of this Regulation is also to ensure that the provisions of Directive 67/548/EEC on the classification, packaging and labelling of substances dangerous to man or the environment when they are placed on the market in the Member States shall also apply to such substances when they are exported from the Member States to third countries.
3. This Regulation does not apply to substances or preparations imported or exported for the purposes of analysis or scientific research and development as defined in Article 2, where the quantities involved are sufficiently small that they are unlikely to affect human health or the environment adversely.

*Article 2: Definitions*

For the purposes of this Regulation, the following definitions shall apply:

1. 'chemical subject to notification'
   means any of the chemical substances listed in Annex I and preparations containing any of these chemicals if the preparation has a labelling obligation under Community legislation as a result of the presence of the Annex I chemical;
2. 'chemical subject to the PIC procedure'
   means each chemical listed in Annex II, whether by itself or in preparations, whether manufactured or obtained from nature, unless its concentration in a preparation is insufficient for a labelling requirement under Community legislation;
3. 'banned chemical'
   means a chemical which has, for health or environmental reasons, been prohibited for all uses by final governmental regulatory action;
4. 'severely restricted chemical'
   means a chemical for which, for health or environmental reasons, virtually all uses have been prohibited by final governmental regulatory action but for which certain specific uses remain authorized;
5. 'export' means:
   (a) the permanent or temporary export of products meeting the conditions of Article 9 (2) of the Treaty,
   (b) the re-export of products not meeting the conditions referred to in (a) which are placed under a customs procedure other than transit procedure;

[1] *Official Journal*, No. L 196 (16.8.1967).
[2] *Official Journal*, No. C 170 (29.6.1988).
[3] London Guidelines for the Exchange of Information on Chemicals in International Trade, Decision 14/27 of the Governing Council of UNEP of 17 June 1987 as amended in May 1989; FAO International Code of Conduct on the Distribution and Use of Pesticides, Rome 1986, as amended in November 1989.

6. 'import'
means the physical introduction into the customs territory of the Community of products which are placed under a customs procedure other than transit procedure;
7. 'prior informed consent' (PIC)
means the principle that international shipment of a chemical which is banned or severely restricted in order to protect human health or the environment should not proceed without the agreement, where such agreements exist, or contrary to the decision of the designated national authority of the importing country;
8. 'reference number'
means the number assigned by the Commission to each chemical subject to notification when it is exported for the first time to a third country. This number remains unchanged for every subsequent export of the same chemical from the Community to the same third country;
9. 'labelling'
means the provision on a label of information related to the potential hazard to health, safety or the environment from use of the chemical. It does not refer to labelling requirements for the transport of dangerous goods.
10. 'scientific research and development'
means scientific experimentation, analysis or chemical research carried out under controlled conditions; it includes the determination of intrinsic properties, performance and efficacy as well as scientific investigation related to product development.

*Article 3: Designation of authorities*

1. Each Member State shall designate the authority or authorities, hereinafter referred to as the 'designated authority' or 'designated authorities', competent for the notification and information procedures laid down by this Regulation. It shall inform the Commission of such designation.
2. As far as the participation of the Community in the international PIC procedure is concerned, the Commission shall act as common designated authority with regard to receiving information from the competent bodies dealing with the international PIC procedure and for providing information to these bodies on common decisions which have been taken in close cooperation and consultation with the Member States in accordance with the provisions of Article 5.

*Article 4: Exports to third countries*

1. When a chemical subject to notification is due to be exported from the Community to a third country for the first time following the date as of which it becomes subject to the provisions of this Regulation, the exporter shall provide the designated authority of the Member State in which he is established, no later than 30 days before the export is due to take place, with the information contained in Annex III necessary to enable the designated authority to effect a notification. The designated authority shall take the necessary measures to ensure that the appropriate authorities of the country of destination receive notification of the intended export. Such notification, which shall as far as possible be made at least 15 days before export, must comply with the requirements set out in Annex III.

Where the export of a chemical relates to an emergency situation in which any delay may endanger public health or the environment in the importing country the provisions referred to above may be waived wholly or partly at the discretion of the designated authority of the exporting Member State.

The designated authority shall send a copy of the notification to the Commission, which shall forward it to the designated authorities of the other Member States and to the International Register of Potentially Toxic Chemicals (IRPTC).

The Commission shall assign a reference number to each notification received and communicate it immediately to the designated authorities of the Member States. It shall periodically publish a list of these reference numbers in the *Official Journal of the European Communities*, stating the chemical concerned and the third country of destination. Until a relevant reference number is published in the *Official Journal of the European Communities*, the exporter shall assume that such an export has not previously taken place unless he can obtain from the designated authority of the Member State in which he is established the relevant reference number previously assigned by the Commission.
2. The designated authority of the relevant Member State shall inform the Commission as soon as possible of any significant reaction from the country of destination. The Commission shall ensure that the other Member States are informed as soon as possible of that country's reaction.
3. For every subsequent export of the chemical concerned from the Community to the same third country, the exporter shall ensure that the export is accompanied by reference to the number of the notification either published in the *Official Journal of the European Communities* or obtained by it from the designated authority of the Member State in which he is established pursuant to the fourth subparagraph of paragraph 1.
4. New notification according to paragraph 1 must be given for exports which take place subsequent to major changes to Community legislation concerning the marketing and use or labelling of the substances in question or whenever the composition of the preparation in question changes to such an extent that the labelling of such preparation is altered. The new notification must comply with the requirements set out in Annex III and must indicate that it is a revision of a previous notification. Information to the effect that a new notification is needed shall be published in the *Official Journal of the European Communities*.

The Commission shall send new notifications to the designated national authorities of countries which have received notification of the export from the Community of the substance or preparation in question in the six months prior to the relevant changes to Community legislation.
5. As regards the transmission of information within the meaning of paragraph 1, the Member States and the Commission shall take account of the need to protect the confidentiality of data and ownership in both the Member States and the countries of destination.

The following shall not be regarded as confidential:
—the names of the substance;
—the names of the preparation;
—the names of substances in Annex I contained in the preparation and their percentage in the preparation;
—the names of the main impurities in the substances in Annex I;
—the name of the manufacturer or exporter;
—information on the precautions to be taken, including the category of danger, the nature of the risk and the relevant warnings;
—physico-chemical data concerning the substances;
—the summary results of the toxicological and ecotoxicological tests;
—the possible ways of rendering the substance harmless;
—the information contained in the safety data sheet;
—the country of destination.

*Article 5: Participation in the international notification and 'prior informed consent' (PIC) procedure*

1. The Commission shall notify the competent bodies dealing with the international PIC procedure of the chemicals which are banned or severely restricted in the Community (Annex I). It shall provide all relevant information, especially on the identity of the chemicals, their dangerous properties, Community labelling requirements and necessary precautionary measures. It shall also identify the relevant control actions and the reasons for them.
2. The Commission shall forward forthwith to the Member States information which it receives regarding chemicals subject to the PIC procedure and the decisions of third countries regarding the imposition of bans or import conditions on these chemicals. The

Commission shall evaluate in close cooperation with the Member States the risks posed by the chemicals. The Commission shall take its decision, including interim decisions, in accordance with the procedure laid down in Article 21 of Directive 67/548/EEC. It shall then inform the IRPTC whether import into the Community of each of the chemicals is allowed, prohibited or restricted.

When such a decision is taken, the following principles shall be observed:

(a) in the case of a substance or preparation banned by Community legislation: import consent for the banned use shall be refused;
(b) in the case of substance or preparation severely restricted by Community legislation: import consent shall be subject to conditions; the appropriate conditions shall be decided on a case by case basis;
(c) in the case of a substance or preparation not banned or severely restricted by Community legislation: import consent shall not normally be refused; however, if the Commission, in consultation with Member States, considers that a proposal should be made to the Council to ban or severely restrict a substance or preparation not produced in the Community, interim import conditions, set on a case by case basis, may be imposed until the Council has taken a decision on the proposed severe restriction or permanent ban.

In the case of a substance or preparation banned or severely restricted by legislation of one or more Member State, the Commission shall, at the written request of the Member State concerned, prepare its decision on the reply to be made to the IRPTC, taking into consideration that Member State's bans or severe restrictions.

The Commission shall, whenever practicable, make use of existing Community procedures and shall ensure that the response does not conflict with existing Community legislation.

3. Annex II shall comprise the following:

(a) the international list of banned and severely restricted chemicals subject to the PIC procedure established by the UNEP and FAO;
(b) a list of the countries participating in the PIC scheme; and
(c) the decisions of these countries (including the Community Member States) regarding the import of the chemicals listed in (a) above.

The Commission shall immediately notify the Member States of information which it receives regarding changes to the above. It shall periodically publish these changes in the *Official Journal of the European Communities*.

4. The exporter shall be required to comply with the decision of the country of destination participating in the PIC procedure.

5. If a participating importing country does not make a response or responds with an interim decision which does not address importation, the *status quo* with respect to imports of the chemical should continue. This means that the chemical should not be exported without the explicit consent of the importing country, unless it is a pesticide which is registered in the importing country or is a chemical the use or importation of which has been allowed by other action of the importing country.

*Article 6: Infringements*

Member States shall take appropriate legal or administrative action in the event of infringement of the provisions of this Regulation.

*Article 7: Packaging and labelling*

1. Dangerous chemicals which are intended for export shall be subject to the measures on packaging and labelling established pursuant to Directive 67/548/EEC or, as appropriate, of other Directives covering dangerous preparations as are applicable in the Member State from which the goods are to be exported or in which they have been produced. This obligation shall be without prejudice to any specific requirements of the importing third country. The label need comply with the requirements of the importing third country only if such requirements ensure that the label has all the health, safety and environment-related information which Community use would require.

2. The information on the label shall as far as practicable be given in the language(s), or in one or more of the principal languages, of the country of destination or of the area of intended use.

*Article 8: Notification from third countries*

1. Where the designated authority of a Member State receives a notification from the competent authority of a third country concerning the export to the Community of a chemical the manufacture, use, handling, consumption, transport and/or sale of which is subject to prohibition or substantial legal restriction under that country's legislation, it shall send forthwith to the Commission a copy of that notification, together with all relevant information.

2. The Commission shall forward forthwith to the Member States any notification received either directly or indirectly, together with all available information.

3. The Commission shall periodically evaluate the information received via the Member States or directly from third countries and, if necessary, submit appropriate proposals to the Council.

*Article 9: Exchange of information and monitoring*

1. Member States shall regularly forward to the Commission information on the operation of the notification system provided for in this Regulation.

2. The Commission shall regularly compile a report on the basis of the information provided by the Member States and forward it to the European Parliament and the Council. This report shall consist of, *inter alia*, information on participation in international notification and PIC systems on the cover provided by such systems and on how they are complied with by third countries.

3. As regards the information supplied pursuant to paragraphs 1 and 2, the Member States and the Commission shall take account of the need to protect the confidentiality of data and ownership.

*Article 10*

If a Member State applies, with respect to substances other than those in Annex I, a national system using similar information procedures in respect of third countries to those laid down in this Regulation, it shall inform the Commission thereof, specifying the substances concerned: the Commission shall forward this information to the Member States.

*Article 11: Updating of Annexes*

1. The list of chemicals in Annex I shall be reviewed by the Commission at regular intervals, particularly in the light of experience gained in implementing this Regulation, with special regard to information received pursuant to Article 10, and on the basis of developments in Community legislation concerning marketing and use and of developments within the framework of the OECD, the UNEP and the FAO. The list shall be amended as necessary by decisions taken by the Council by qualified majority on a proposal from the Commission.

In determining whether regulatory action qualifies as a ban or severe restriction, the effect of the action on any one of three major use categories must be considered. These categories are:

(a) plant protection products;
(b) industrial chemicals;
(c) consumer product chemicals.

If, for health or environmental reasons, the control action bans or severely restricts the use of a chemical in any one of these categories of use, it will be included in Annex I.

2. Amendments initiated by the UNEP and the FAO to the list of chemicals subject to the international PIC procedure and to the PIC decisions of importing countries (Annex II) shall be

adopted in accordance with the procedure laid down in Article 21 of Directive 67/548/EEC.

3. The amendments required for adapting Annex III to scientific and technical progress shall be adopted in accordance with the procedure laid down in Article 21 of Directive 67/548/EEC.

*Article 12*

1. Regulation (EEC) No 1734/88 is hereby repealed.
2. References to Regulation (EEC) No 1734/88 shall be construed as references to this Regulation.

*Article 13*

This Regulation shall enter into force three months from the day of its publication in the *Official Journal of the European Communities*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 23 July 1992

*ANNEX I*

*List of chemicals banned or severely restricted to certain uses by Community legislation owing to their effects on health and environment*

| Chemical | CAS No. (a) | EINECS No. (b) | Use category (c) | Use limitation (d) |
|---|---|---|---|---|
| 1. Mercuric oxide | 21908-53-2 | 244-654-7 | p | sr |
| 2. Mercurous chloride (calomel) | 10112-91-1 | 233-307-5 | p | sr |
| 3. Other inorganic mercury compounds | | | p | b |
| 4. Alkyl mercury compounds | | | p | sr |
| 5. Alkoxyalkyl and aryl mercury compounds | | | p | b |
| 6. Aldrin | 309-00-2 | 206-215-8 | p | sr |
| 7. Chlordane | 57-74-9 | 200-349-0 | p | b |
| 8. Dieldrin | 60-57-1 | 200-484-5 | p | b |
| 9. DDT | 50-29-3 | 200-024-3 | p | b |
| 10. Endrin | 72-20-8 | 200-775-7 | p | sr |
| 11. HCH containing less than 99% of the gamma isomer | 608-73-1 | 210-168-9 | p | b |
| 12. Heptachlor | 76-44-8 | 200-962-3 | p | b |
| 13. Hexachlorobenzene | 118-74-1 | 204-273-9 | p | b |
| 14. Camphechlor (toxaphene) | 8001-35-2 | 232-283-3 | p | b |
| 15. Polychlorinated biphenyls (PCB), except mono- and dichlorinated biphenyls | 1336-36-3 | 215-648-1 | i | b |
| 16. Polychlorinated terphenyls (PCT) | 61788-33-8 | 262-968-2 | i | b |
| 17. Preparations with a PCB or PCT content higher than 0.01% by weight | | | i | b |
| 18. Tris (2,3-dibromopropyl) phosphate | 126-72-7 | 204-799-9 | i | sr |
| 19. Tris-aziridinyl-phosphinoxide | 545-55-1 | 208-892-5 | i | sr |
| 20. Polybrominated biphenyls (PBB) | | | i | sr |
| 21. Crocidolite | 12001-28-4 | | i | sr |
| 22. Nitrofen | 1836-75-5 | 217-406-0 | p | b |
| 23. 1,2 Dibromoethane | 106-93-4 | 203-444-5 | p | b |
| 24. 1,2 Dichloroethane | 107-06-2 | 203-458-1 | p | b |

(a) CAS = Chemical Abstracts Service.
(b) EINECS = European Inventory of Existing Commercial Chemical Substances.
(c) Use category = p: plant-protection product; i: industrial chemical.
(d) Use limitation = sr: severe restriction; b: ban.

*ANNEX II*

Chemicals subject to the international PIC procedure and the PIC decisions of importing countries [Article 5(3), (a), (b) and (c)]

*ANNEX III*

*Information required pursuant to Article 4*

1. Identity of the substance or preparation to be exported:

1.1 *Substances:*
—name in nomenclature of the International Union of Pure and Applied Chemistry,
—other names (usual name, trade name, abbreviation),
—EINECS-number and CAS-number, if available,
—main impurities of the substance, when particularly relevant.

1.2 *Preparations:*
—trade name or designation of the preparation,
—for each substance listed in Annex I, percentage and details as specified under 1.1.

2. Information on precautions to be taken, including category of danger and risk and safety advice.
3. The name address, telephone and telex or fax numbers of the designated authority from which further information may be obtained.
4. Summary of regulatory restrictions and reasons for them.
5. Expected date of first export.
6. Reference number.
7. Country of destination.
8. Use category.
9. Estimated amount of the chemical to be exported to the destination country in the next year if possible.

The above information should be provided on an expert notification form as shown hereafter.

*Source: Official Journal of the European Communities*. L 251, Vol. 35 (29 August 1992).

## International Agency for Research on Cancer

World Health Organization
Lyon-France

### Fellowships for research training in cancer 1994-1995

**Applications for training fellowships in 1994-1995 are invited from junior scientists wishing to be trained in those aspects of cancer research related to the Agency's own programmes: epidemiology, biostatistics, environmental and viral carcinogenesis and mechanisms of carcinogenesis. Applications are encouraged from epidemiologists and laboratory scientists for interdisciplinary training that will facilitate the conduct of genetic and molecular epidemiological research. Applicants requiring basic training in cancer epidemiology will also be considered.**

Applicants should be engaged in research in medical or allied sciences and intend to pursue a career in cancer research.

Fellowships are awarded for one year and are tenable at the Agency or in any other suitable institution abroad. Fellows will, in general, be selected from applicants with some postdoctoral research experience related to cancer in medicine or the natural sciences. Applicants must have an adequate knowledge, both written and spoken, of the language of the country in which their fellowship is tenable.

Applications cannot be accepted from people already in receipt of funds enabling them to study abroad or who are already in their proposed host institute prior to the selection.

Stipends will vary according to the cost of living in the country of study. The cost of travel for the applicant, and in certain circumstances, that of one dependent, will be met.

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*Fellowship application forms and more detailed information are available from:*

**Education and training programme**
International Agency for Research on Cancer
150 cours Albert-Thomas, 69372 Lyon Cedex 08, France

**Applications must reach the Agency no later than 31 December 1993.**

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